



### September 2009

### **NIEHS Spotlight**



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During a town meeting August 3, NIEHS launched a "wide open" search for its next scientific director and head of the

Division of Intramural Research (DIR). ...read more



# **Kington Honors NIEHS Employees**

Twelve NIEHS employees were among recipients of 2009 Director's Awards presented by NIH Acting Director Raynard Kington, M.D., Ph.D., at a

ceremony July 29 in Bethesda, Md. ...read more



#### Collins Begins Tenure as Director with Town Meeting

Shortly after being sworn in on his first day at the helm of NIH, Director Francis Collins, M.D., Ph.D., spoke at an all-hands town meeting August 17

in the Main Auditorium at Natcher Auditorium on the NIH campus in Bethesda, Md. ....read more



# Birnbaum Opens Workshop on Epigenetics

NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., presented opening remarks at the National Academies workshop

on epigenetics July 30–31 at the organization's Keck Building in Washington. ...read more

#### **Science Notebook**



# Aging Research Yields Promising Medical Compounds

Harvard School of Medicine Professor David Sinclair, Ph.D., concluded the 2008-2009 NIEHS

Distinguished Lecture Series on August 11 with a thought-provoking seminar titled "Pathways That Control the Pace of Aging and Disease: Prospects for New Medicines." NIEHS Principal Investigator Xiaoling Li, Ph.D., hosted the talk, which drew a capacity audience. ...read more



# **Summer Students Explore Basics of Epidemiology**

In the last interactive Summers of Discovery seminar of the year on August 5, NIEHS Epidemiology Branch Chief Dale Sandler, Ph.D.,

and Senior Investigator Allen Wilcox, M.D., Ph.D., worked as a team to give the students "a taste of epidemiology.". ...read more



# Superfund Study of Carbon Nanoparticle Toxicity in Adult Flies

Researchers at Brown University's NIEHS-funded Superfund Research Program (Brown SRP)

report in the latest edition of *Environmental Science* and *Technology* that carbon nanoparticles cause a significantly higher mortality rate in adult fruit flies than in very young flies. ....read more

### **NIEHS Spotlight**



## 2009 Summers of Discovery Best Poster Awards

Michelle Corea, John Peart, and Amber Haynes, interns in the Summers of Discovery Program, won Best Poster awards for their

summer research at a ceremony on July 29.
NIEHS Deputy Scientific Director Bill Schrader, Ph.D.,
presented the awards. ...read more



# Gohlke Awarded AAAS Policy Fellowship

The American Association for the Advancement of Science (AAAS) announced in August that NIEHS Postdoctoral Fellow Julia Gohlke,

Ph.D., has been selected to participate in its prestigious Science and Technology (S&T) Policy Fellows program during 2009-2010. ....read more



# NIEHS Joins Supporters of African Toxicology Meeting

NIEHS is helping to advance the understanding of toxicology in Africa with a \$15,000 donation to support an environmental risk assessment

training workshop at the 7th Congress of Toxicology in Developing Countries (CTDC). ...read more



# **Linking the Built Environment and Obesity**

NIEHS hosted the third and final meeting of grantees in the Obesity and Built Environment (OBE) Program, which was funded by NIEHS and partner agencies.

August 13-14 in Rodbell Auditorium. ....read more



## **Kindergartners Give to Two Sister Study**

This summer NIEHS Director Linda Birnbaum, Ph.D., received a donation for the Two Sister Study from a kindergarten class at Coleytown

Elementary School in Westport, Conn. . ....read more

#### **Science Notebook**



# Epigenetic Changes Associated with Prenatal Tobacco Exposure

A new NIEHS-funded study published by researchers at the University of Southern California (USC) reports that

life-long effects of prenatal exposure to tobacco may be mediated by changes in DNA methylation. ....read more



#### Research Suggests Viral Protein Manipulates Host Cells to Cause Flu-like Symptoms

In response to the current H1N1 pandemic, the scientific community has increased its efforts to better

understand how influenza virus spreads and how to mediate its adverse health effects. ...read more



#### Wilson Chairs Gordon Conference on Genetic Toxicology

NIEHS Laboratory of Structural Biology (LSB) Principal Investigator Samuel Wilson, M.D., served as

the chair of the 2009 Gordon Conference on Genetic Toxicology August 9–14 at Colby-Sawyer College in New London, NH. ...read more



## An NTP Caveat — Predictive Toxicity and Nanomaterials

In a forum series article published in the August issue of *Toxicological Sciences*, National Toxicology Program (NTP) Deputy Program

Director for Science Nigel Walker, Ph.D., and NTP Associate Director John Bucher, Ph.D., take a critical look at the 21st century paradigm for evaluating the health hazards of nanoscale materials. ...read more



#### This Month in EHP

The August issue of *Environmental Health Perspectives (EHP)* highlights H1N1 influenza with a Focus article on the possible role of concentrated animal feeding operations (CAFOs).

...read more

### **NIEHS Spotlight**



## A Stimulating Summer for Intern Amber Haynes

Thanks to the American Recovery and Reinvestment Act (ARRA), the 2009 NIEHS Summers of Discovery Program may prove to be a turning point for

aspiring physician-scientist Amber Haynes. ...read more



## **Bushel and Paules to Present at Toxicogenomics Meeting**

NIEHS scientists Pierre Bushel, Ph.D., and Rick Paules, Ph.D., will join colleague Weida Tong, Ph.D., as U.S. representatives at the Joint Symposium of

the 5th International Conference on Toxicogenomics (ICT) and 2nd Toxicogenomics Integrated Environmental Science (TIES) in Seoul, Korea September 20–23. ....read more



# **Environmental News Organization Seeks Fellowship Applications**

Environmental Health Sciences (EHS), a non-profit environmental news publisher, is accepting nominations through

October 15 for ten 12-month appointments to its 2010 Science Communications Fellows program. ....read more

### **Inside the Institute**



#### A Community of Support for the Summers of Discovery Students

For this year's Summers of Discover interns, the July 29 Poster Session was the culmination of four to six weeks of

experimental research. ...read more



## **Employees Recognized for Decades of Service**

In another first for NIEHS and the National Toxicology Program, Director Linda Birnbaum, Ph.D., honored employees for their decades of service

with their own dedicated ceremony and reception in Rodbell Auditorium August 7. ...read more

#### **Science Notebook**



# Birnbaum To Give Distinguished Lecture September 8

NIEHS opens its 2009–2010 Distinguish Lecture Series on September 8 with a talk on

"Halogenated Flame Retardants: Does the Benefit Justify the Risks?" by NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D.. ...read more

#### **Extramural Research**

#### **Extramural Update**

As part of its Small Business Innovation Research (SBIR) program, on August 17 the National Institutes of Health (NIH) in conjunction with the Centers for Disease Control and Prevention (CDC) published a Request for Proposals (RFP) SBIR Contract Solicitation in the Federal Register. ...read more

#### **Extramural Papers of the Month**

- · "Sloppier Copier" Mysteries Solved
- Bisphenol A Reduces the Effectiveness of Chemotherapeutics
- Progesterone Triggers Breast Inflammation
- Potential Discovery of New Asthma Therapy

### Intramural Research

#### **Intramural Papers of the Month**

- RAP80, Part of an Autoregulatory Loop with HDM2 and p53, Enhances p53 Degradation
- Alpers Disease Mutations In Polymerase Gamma Impair Mitochondrial DNA Replication
- Mi-2/NuRD Is Part of a Novel Chromatin Assembly Pathway
- Web-Based SNP Tools Offer Unique Usability Features

### Inside the Institute



## Work/Life Event Focuses on Community Resources

NIEHS held its most recent Work/Life event on August 6 with a mid-day Community Resources Festival in Rodbell Auditorium. ....read more

### **Calendar of Upcoming Events**

- September 1–October 2 (Offsite Event), at the Durham County Main Library in Durham, during library hours "Harry Potter's World: Renaissance Science, Magic, and Medicine," a traveling exhibition for libraries organized by the National Library of Medicine
- **September 1**, Rodbell A, 11:00–12:00 Biostatistics Branch Seminar on "Systems Biology and Epigenetics of Gene Regulation," by Raja Jothi, Ph.D.
- **September 1**, Rodbell Auditorium, 1:00–3:30 NIEHS Genomics Day, featuring lectures followed by a poster session
- **September 8**, Rodbell Auditorium, 11:00–12:30 Distinguished Lecture by Linda Birnbaum, Ph.D., on "Halogenated Flame Retardants: Does the Benefit Justify the Risk?"
- September 10 (Webcast event), at NIH, Bethesda, 1:00–3:00 "Sex and Gender Research: The Interaction of Depression with Other Diseases," featuring talks by Jill Goldstein, Ph.D., Giovanni Cizza, M.D., Mary Jane Massie, M.D., and Viola Vaccarino, M.D., Ph.D.
- September 14–18 (Offsite Event), at Lake Tahoe Green Technology Entrepreneurship Academy
- September 15–16, Rodbell Auditorium, 8:30–5:00 National Advisory Environmental Health Sciences Council (NAEHSC) meeting
- **September 17**, Rall Building D-450, 10:00–11:00 Laboratory of Molecular Carcinogenesis Seminar on "Chromatin and transcription," by Trevor Archer, Ph.D.
- **September 24**, Rall Building D-450, 10:00–11:00 Laboratory of Molecular Carcinogenesis Seminar on "Understanding and designing gene regulation by PUF proteins" by Traci Hall, Ph.D.
- September 24–25 (Webcast event), at NIH Masur Auditorium, Bethesda Fifth Annual NIH Director's Pioneer Award Symposium
- View More Events: NIEHS Public Calendar

# **NIEHS Spotlight**

## **Grady Chairs "Wide Open" Search for NIEHS Scientific Director**

By Eddy Ball

During a town meeting August 3, NIEHS launched a "wide open" search for its next scientific director and head of the Division of Intramural Research (DIR). Fresh from an extended meeting with NIEHS Director Linda Birnbaum, Ph.D., members of the search committee chaired by National Institute of Nursing Research Director Patricia Grady, Ph.D. (see text box) fielded questions and comments from NIEHS employees on what the Institute needs from its chief scientific leader — and how best to spread word of the opening as widely as possible.

On August 24, NIH issued the official announcement of the opening, and NIEHS began placing advertisements in major medical and environmental journals. Closing date for applications is December 1, 2009.

Grady opened the meeting by assuring the audience, "Nothing is off the table." She also encouraged people to suggest possible candidates to the committee. "The key right now is to get the word out," she said. "The issue is for you to help us identify people who would be good candidates for this job."



Search Committee Chair Patricia Grady (Photo courtesy of NIH)

As she explained, the successful candidate will be an accomplished senior scientist or principal investigator with an M.D., Ph.D. or equivalent degree who is willing and able to devote most of his or her time as scientific director to administration and fostering the career development of others. Comments from audience members also emphasized that the new leader should have a well articulated vision of interdisciplinary research at the Institute, be an inspiring leader with a commitment to sustainability and possess effective science communication skills for serving as the "public face" of DIR.

Tom Kunkel, Ph.D., an NIEHS principal investigator, said at the close of the session, "I've never seen a meeting of this kind." The town hall meeting was the first time that NIEHS staff members have been invited to express their thoughts to the selection committee on skills and personal attributes they hope to see in the next scientific director.

Birnbaum has said several times that she wants a scientific director who will consider the best interests of all NIEHS programs — not merely the DIR, its 850 employees, and 17 laboratories and branches, including its new Clinical Research Unit. The candidate, according to Birnbaum, will be a key member of the NIEHS leadership team, helping to guide the Institute in pursuit of its research excellence and public health mission.

#### **NIEHS Scientific Director Search Committee**

The search committee is a diverse group of people from NIEHS, other NIH institutes and centers, and scientists from other institutions with what Grady called "a breadth of expertise" reflecting the wide range of research at NIEHS:

- Search Committee Chair Patricia Grady, Ph.D., director, National Institute of Nursing Research /NIH
- Eric Green, M.D., Ph.D., scientific director, National Human Genome Research Institute/NIH
- Joseph Fraumeni, M.D., scientific director, National Cancer Institute (NCI)/NIH
- Joan Schwartz, Ph.D., assistant director Office of Intramural Research, NIH
- Frank Gonzalez, Ph.D., Lab Chief, NCI/NIH
- David Peden, M.D., director, Center for Environmental Medicine, Asthma and Lung Biology Chief, Division of Allergy, Immunology and Environmental Medicine, School of Medicine Professor, Department of Pediatrics School of Medicine, University of North Carolina at Chapel Hill (UNC-CH)
- Kenneth Ramos, Ph.D., professor, Department of Biochemistry and Molecular Biology Director, Center for Genetics and Molecular Medicine School of Medicine, University of Louisville
- Michael Gallo, Ph.D., professor, Department of Environmental and Occupational Medicine, director of EOHSI's NIEHS Center for Environmental Health Sciences Director, Toxicology Division University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School
- Barbara Rimer, DrPH, dean and Alumni Distinguished Professor, Gillings School of Global Public Health UNC-CH
- Tom Kunkel, Ph.D., director, Environmental Biology Program Chief, Laboratory of Structural Biology NIEHS/NIH
- Dori Germolec, Ph.D., biologist, Toxicology Branch, National Toxicology Program NIEHS/NIH
- Dale Sandler, Ph.D., chief, Epidemiology Branch Head, Chronic Disease Epidemiology Group NIEHS/NIH
- Gwen Collman, Ph.D., acting director, Division of Extramural Research and Training NIEHS/NIH

#### **Ex Officio Members:**

- Ms. Stephanie Jones Branch Chief, Human Resources, OD/NIH
- Ginny Ivanoff, EEO Specialist, OEO, OD/NIH
- Lisa Rogers Administrative Officer, DIR, NIEHS

## **Kington Honors NIEHS Employees**

By Eddy Ball

Twelve NIEHS employees were among recipients of 2009 Director's Awards presented by NIH Acting Director Raynard Kington, M.D., Ph.D., at a ceremony July 29 in Bethesda, Md.

Epidemiology Branch Chief Dale Sandler, Ph.D., received a Scientific Medical Award for her role as principal investigator of the Sister Study. Program Analyst Liam O'Fallon was recognized with an Administrative Award for his work with the Partnerships for Environmental Public Health (PEPH) initiative. Kington presented an Administrative Award to the seven members of the NIEHS Water Crisis Task Force — Bill Blair, Vicky Englebright, Deborah Gaffney, Gregory Holland, Scott Merkle, Dick Sloane and Mitch Williams.

Former Director of Education and Biomedical Research Marian Johnson-Thompson, Ph.D., and Ebony Bookman, Ph.D., were recognized for their contributions to the first NIH Summit: The Science of Eliminating Health Disparities held Decmber 16–18, 2008. Chief of the Scientific Review Branch Terry Nesbitt, D.V.M., Ph.D., was a member of a trans-NIH group honored for their efforts in the Early Stage Investigator Workgroup.





Birnbaum, left, Sandler and Kington, right, posed on stage with the award. Sandler oversees the Sister Study, which reached its 50.000 subject enrollment goal this summer. (Photo courtesy of NIH)



Birnbaum, left, Williams and Kington are shown on the awards stage. Williams accepted the award on behalf of the NIEHS Water Crisis Task Force. (Photo courtesy of NIH)

O'Fallon was instrumental in organizing the highly successful PEPH meeting in July 2008. The program announced its first Requests for Applications in February 2009. (Photo courtesy of Steve McCaw)



During her 14-year career at NIEHS, Johnson-Thompson pursued a mission to expand science education opportunities for minorities and underserved populations. Photo courtesy of Steve McCaw)



Bookman has served as acting director of Education and Biomedical Research since Johnson-Thompson's retirement in September 2008. (Photo courtesy of Steve McCaw)

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## **Collins Begins Tenure as Director with Town Meeting**

By Eddy Ball

Shortly after being sworn in on his first day at the helm of NIH, Director Francis Collins, M.D., Ph.D., spoke at an all-hands town meeting August 17 in Natcher Auditorium on the NIH campus in Bethesda, Md. The meeting, which was webcast, gave Collins an opportunity to outline his vision for the future of NIH in broad strokes and single out the major challenges he sees ahead.

The ceremony opened with a standing ovation of thunderous applause for the new director. Deputy Director Raynard Kington, M.D., Ph.D., introduced Collins, describing him as an "international hero" and "brilliant choice" to serve as the agency's 16th director. He noted that Collins in his role as director of the National Human Genome Research Institute oversaw the human genome project, which was completed ahead of schedule and under its projected budget.

Collins was clearly on familiar turf as he talked about his long history with NIH. He called the organization "the most amazing, creative place to do biomedical research in the world [and] not just a collection of brilliant minds," but also "a brilliant collection of minds." He praised the NIH as more than a community or even a family, and midway in his talk he began referring to the "NIH tribe."



Collins called addressing health disparities "a high priority for NIH" and emphasized his support for the Intramural program. "I am one of you." (Photo courtesy of NIH)

Collins cautioned his audience that he would speak generally and meant no one any slight by omission, focusing on five areas that he sees as important for the future of NIH:

- The exploitation of high-throughput technologies to answer "questions we couldn't answer before," including the cancer genome atlas, complex disease and the microbiome.
- Translating research into practicing, expediting drug development and exploring the potential of stem cells.
- Putting science to work for the benefit of health care reform with such efforts as increased comparative effectiveness research, personalized medicine and pharmacogenomics.
- Placing greater emphasis on global health and seizing the opportunity for the U.S. to become "a doctor to the world."
- Striving to stabilize the biomedical research community with steady funding post-stimulus and to improve prospects for young researchers.

Along with presenting himself to the NIH "tribe" as a seasoned member of the scientific community dedicated to focusing "full energies on NIH," Collins reassured his audience, "I will step aside from other activities." He emphasized, "I don't want anyone to think that I have a religious agenda" for NIH. Decisions will be based on science, he said, comparing himself to the conductor of an "orchestra" of scientists with different research interests, as he committed himself to the total scientific interests of the agency.

"The world is waiting," he urged his listeners before taking questions. "Let us begin."

As director of the NIH, Collins will bear responsibility for more than 19,000 employees and a fiscal year 2009 budget of \$30.6 billion. NIH supports more than 325,000 researchers at more than 3,100 institutions in the US and worldwide.

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# Birnbaum Opens Workshop on Epigenetics

By Eddy Ball

NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., presented opening remarks at the National Academies workshop on epigenetics July 30–31 at the organization's Keck Building in Washington. The theme of the meeting was "Use of Emerging Science and Technologies to Explore Epigenetic Mechanisms Underlying the Developmental Basis for Disease," with several NIEHS-funded scientists on hand to offer their perspectives on the issues.

Birnbaum's overview at the meeting, "Developmental Basis of Disease: A New Paradigm in Environmental Health Sciences," opened with a reference the Barker hypothesis, which proposes that abnormal developmental diet could lead to increased susceptibility



The National Academies Keck Building in downtown Washington (Photo courtesy of the National Academies)

to disease later in life. She noted a recent shift in focus of teratology studies — investigations into abnormal development —which has moved from the immediate and short term "apical" endpoints of death, birth defects and low birth weight to encompass later adverse health outcomes of early exposure to chemicals. She said that this broadening range of concern and new technologies have triggered a paradigm shift in toxicology.

"While people talked about functional changes [before]," Birnbaum explained, "we did not know how to measure them until the use of 'omics technology allowed us to 'see' functional changes at the gene expression and proteomics level." It became increasingly evident, she continued, that developmental exposure — *in uteri* and neonatal — can lead to increased susceptibility to disease by alterations in programming, which set the stage for abnormal tissue development and disease later in life.

Recognizing the developmental basis of disease, Birnbaum continued, "changes everything,... [shifting] the focus from curing a disease to prevention and intervention strategies to reduce disease occurrence." It offers opportunities for prevention and intervention strategies by offering the possibility of discovering "an 'imprint' left by developmental programming such as altered methyl marks," she explained, that may be useful for identification of exposed individuals and as a biomarker for disease susceptibility."

Birnbaum closed her talk with the questions that would occupy attendees at the workshop. She challenged her audience to understand better what changes are occurring and what the most sensitive life stages are; to discover whether epigenetic alterations are correlative or causative and what tools need to be developed to characterize the relationships between early exposures and outcomes years or even generations later; and to determine the implications for disease prevention, regulation and interventions in this generation and the next.

Participating as panelists were NIEHS Associate Director in the Office of Risk Assessment Research Chris Portier, Ph.D., and Principal Investigator and Chief of the Laboratory of Molecular Carcinogenesis Trevor Archer, Ph.D. NIEHS grantee Wan-yee Tang, Ph.D., of the University of Cincinnati made a presentation on "Epigenetic Markers for Transplacental Exposure to Airborne Polycyclic Aromatic Hydrocarbons and Childhood Asthma." Superfund Research Program grantee Kim Boekelheide, Ph.D., of Brown University, served as a panelist.



According to Birnbaum, the new paradigm of toxicology extends the window of adverse health effects by years and even generations into the future and back into the past. (Photo courtesy of Steve McCaw)



Portier was on hand to offer his perspective on regulatory and communication implications. (Photo courtesy of Steve McCaw)

The workshop was part of the National Academies series on "Emerging Science for Environmental Health Decisions." The series continues with a meetings in Washington on "Computational Toxicology: From Data to Analyses to Applications" September 21–22 and on "The Exposome: A Powerful Approach for Evaluating Environmental Effects on Chronic Diseases" December 8–9.



Archer was a panelist discussing development of screening tools. (Photo courtesy of Steve McCaw)



Tang also participated in the panel discussion on knowledge gaps. (Photo courtesy of Shuk-mei Ho and the University of Cincinnati)

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## **2009 Summers of Discovery Best Poster Awards**

By Laura Hall

Michelle Corea, John Peart, and Amber Haynes, interns in the Summers of Discovery Program, won Best Poster awards for their summer research (see text box) at a ceremony on July 29. NIEHS Deputy Scientific Director Bill Schrader, Ph.D., presented the awards.

In all, 41 posters were judged by postdoctoral fellows who evaluated each of the intern's presentations. Judging was based on the quality of the research and a demonstrated understanding of the work, and how well the research was communicated (see related Inside story). Speaking to the interns, Diane Klotz, director of the Office of Fellows' Career Development, said she chose fellows as judges "because I actually find the post docs to be a lot more critical." She added, "All the judges that I talked to were very impressed with all of your posters, every single one" and "they were just incredibly impressed [with] those of you who are in high school."



Corea, left, received Best Poster award for high school students from Schrader. Corea said, "My biggest interest is in cancer research and epidemiology, but I think this summer helped [me] to broaden my horizons." (Photo courtesy of Steve McCaw)

Before he gave out the awards, Schrader said, "I hope this [the Summers of Discovery experience] helps to trigger your real interest in science." These three winners are definitely intrigued. Corea has thought about medical school, research, and entering an M.D.-Ph.D. program for her future career. Now at the end of her summer internship she says, "I'm leaning towards research."

Peart, a North Carolina State University (NCSU) undergraduate, will continue working with his summer mentor, Ron Cannon, Ph.D., a staff scientist in the NIEHS Intracellular Regulation Group headed by David Miller, Ph.D. Peart will be working full-time in the laboratory for the entire 2009 fall semester as an NCSU Co-op student. The NCSU Co-op program allows students to work in a job relevant to their studies as part of their university curriculum.

Peart's reason to participate in the Co-op program was not just to make himself a better job candidate — he was hooked. "The project we're doing now is continuing on...and it would be really cool to see what the results are, to see it through to the end, keep it going and answer the questions we don't have the answers to yet."



Haynes, left, received graduate Best Poster award from Schrader. In talking about her summer Haynes said, "I always wanted to do research like this because... when you're doing research, particularly in public health, you're able to change thousands of people's lives by just this one thing." (Photo courtesy of Steve McCaw)

# **Summers of Discovery Award Winning Posters**

High school student Corea studied metastasis associated protein 3 (MTA3), a protein involved in regulating gene expression. Her work suggested MTA3 might also be involved in sub-cellular component recycling. This kind of recycling would make nutrients available and potentially increase survival during starvation. Biologist Wendy Jefferson in the Reproductive Medicine Group mentored Corea.

Peart, a North Carolina State University (NCSU) undergraduate, studied an efflux transporter, p-glycoprotein (P-gp) in the blood brain barrier. P-gp is one of the major obstacles preventing drug delivery to the brain. Peart found that sphingosine-1-phosphate (S1P), a lipid signaling molecule, can reversibly down regulate P-gp transport activity making S1P a good candidate for further study in the search for compounds useable for therapeutic drug delivery in brain disease. Ron Cannon, Ph.D., staff scientist in the Intracellular Regulation Group, mentored Peart.

Haynes, a graduate school student in the epidemiology department of Tulane University, worked with Michelle Sever, biologist, and Darryl Zeldin, M.D., acting director of clinical research and principal investigator, in the Laboratory of Respiratory Biology. She tested whether the use of in-home dust mite allergen test kits that allow parents to test for dust mite levels in the home, would, with prevention education, reduce the dust mite levels in the homes of children with allergies to dust mites. Haynes found a significant decrease in dust mite levels reported by the study participants with prevention education and kits over an eight eight-month time period.

Amber Haynes was so interested in her summer project she asked to stay on at NIEHS for another year to continue research on behavioral modification and asthma prevention (see related Spotlight story). "Even though we have preliminary results, I'd like to see what the results will be from the [home dust] samples that were collected and to look at other allergens," said Haynes.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)

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Peart, left, received the undergraduate Best Poster award from Schrader. Peart said that the process of making the poster "taught me how to be professional in writing and how the publication process works." (Photo courtesy of Steve McCaw)

## **Gohlke Awarded AAAS Policy Fellowship**

By Eddy Ball

The American Association for the Advancement of Science (AAAS) announced in August that NIEHS Postdoctoral Fellow Julia Gohlke, Ph.D., has been selected to participate in its prestigious Science and Technology (S&T) Policy Fellows program during 2009-2010. She will work as an AAAS Diplomacy Fellow in the U.S. State Department Office of Global Change following a two-week orientation organized by AAAS that began on September 1.

Gohlke worked with NIEHS Associate Director Chris Portier, Ph.D., during her tenure at NIEHS in the Laboratory of Molecular Toxicology. She pursued policy interests in energy sustainability, climate change, children's health, quantification of human health impacts, risk assessment for global threats, life cycle analysis and cost-benefit analysis.

Gohlke was among representatives from NIEHS at several high-profile meetings and workshops on global health, including the January 2008 National Council for Science and the Environment Climate Change: Science and Solutions conference in Washington and the December 2008 International EcoHealth Forum in Merida, Mexico. She has published several peer-reviewed studies during her time at NIEHS in molecular toxicology and systems approaches to human health research.



Gohlke is one of the 190 Fellows in the 2009-2010 cohort — the largest in the history of the program. (Photo courtesy of Steve McCaw)

Since the program began in 1973, nearly 2,200 scientists and engineers have participated in AAAS Science & Technology Policy Fellowships. Some have gone back to the laboratory or science classroom. But many have established new careers in government or with policy-oriented organizations. According to AAAS, the Fellows program continues to grow as more and more government agencies seek scientific expertise. In fact, the demand for S&T experts far outweighed the number of finalists in the program.

NIEHS scientists and fellows who have participated in the S&T Policy Fellows program include Principal Investigator Traci Hall, Ph.D., and former Laboratory of Molecular Genetics Fellow John Fortune, Ph.D., who now works at the Department of Homeland Security (DHS) as a program manager in the Science and Technology Directorate's Infrastructure and Geophysical Division.

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## **NIEHS Joins Supporters of African Toxicology Meeting**

By Eddy Ball

NIEHS is helping to advance the understanding of toxicology in Africa with a \$15,000 donation to support an environmental risk assessment training workshop at the 7th Congress of Toxicology in Developing Countries (CTDC). The event will be held September 6–10 in Sun City, South Africa. The workshop was organized by the African Society for Toxicological Sciences (ASTS) and co-sponsored by ASTS and Toxicology Excellence for Risk Assessment (TERA).



ASTS President Sanmi Areola, Ph.D., said of the donation, "Continuing support for ASTS activities by NIEHS is creating invaluable opportunities for African scientists in facilitating exposures to modern concepts of toxicology and environmental health sciences." NIEHS funds will help offset the costs of stipends for attendees.

The Congress features a program of continuing education courses, symposia and workshops designed to introduce scientists in developing countries to the principles of toxicology and pathology. NIEHS support will help maximize resources through partnerships with other organizations in an effort to develop indigenous infrastructure for advancing environmental health sciences in the region.

Held every three years, the congresses are sponsored by the International Union of Toxicology (IUTOX). The meetings provide a forum for discussing toxicological problems facing developing countries in the future and exchanging views with toxicologists from all over the world, especially from developing countries and regions. The two most recent CTDCs were held in Guilin, China in 2003 and Cavtat/Dubrovnik, Croatia in 2005.



Areola was photographed in his office at the Nashville, Tenn. Department of Health. (Photo courtesy of Sanmi Areola)

Support for the CTDCs also comes from American groups, such as the American College of Medical Toxicology and Society of Toxicology. Foreign and international supporters include the International Council for Science (ICSU) Regional Office for Africa, the Cancer Association of South Africa (CANSA), the Gesellschaft für Toxikologie (GT), the Federation of European Toxicologists & European Societies of Toxicology (EUROTOX), and the Academy of Sciences for the Developing World (TWAS).

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## **Linking the Built Environment and Obesity**

By Eddy Ball

NIEHS hosted the third and final meeting of grantees in the Obesity and Built Environment (OBE)

Program, which was funded by NIEHS and partner agencies, August 13–14 in Rodbell Auditorium.

Ten of the grantees — six of them funded in whole or part by NIEHS — were on hand to share their challenges, successes and inevitable frustrations during a workshop moderated by NIEHS Health Science Administrator Michael Humble, Ph.D.

Humble opened the meeting with a working definition of the built environment. "Basically, the built environment includes all the building spaces, all the products that are created by people — your homes, the places where you work, the playgrounds in your neighborhoods, transportation."

In their various programs, the grantees strive to better understand how modifiable aspects of the built environment can influence overweight and obesity among residents and how those factors may be manipulated to improve public health. Topics of the grantees' reports ranged from the quality of sidewalks, public transportation and recreational facilities to the prevalence of fast food outlets and liquor stores, perception of neighborhood quality and safety, and fresh vegetable availability.

One team found a significant impact of the new light rail system in Charlotte, N.C. on residents' physical activity and body mass index with potential public health savings, while another equipped young people living in the bi-national twin cities of El Paso, Tex. and Cuidad Juarez, Mexico with personal detection devices to measure food intake and physical activity patterns. A project based at Dartmouth College delineated environmental and family influences on



NIEHS colleagues Humble, center, and Dilworth listened to a presentation by John MacDonald, Ph.D., of Rand Health, on the cobenefits of light rail in Charlotte. (Photo courtesy of Steve McCaw)



NIEHS grantee Amy Schultz noted that a squad car police presence on greenways in Detroit sent untended messages to residents — instead of communicating that the greenway was safe, squad cars implied the area may be dangerous. (Photo courtesy of Steve McCaw)

adolescent overweight in rural New England, while a team in Portland, Ore. mapped urban neighborhoods based on land mixed use patterns and examined the influence on the physical activity, overweight and obesity, and blood pressure of elderly residents.

Along with expanding the literature base on OBE and honing research methodology, the research has energized educational and public policy efforts with hard data about the link between where people live and how healthy they are. A field that is still in its early stages, OBE research needed to develop effective evaluation tools, identify data bases, and characterize surveillance and intervention strategies — major goals of projects in the Boston area, Seattle and San Diego.

In Detroit's Lean and Green in Motown project, investigators gained insight into what shapes residents' perception of the safety of greenways, a major outlet for exercise, and staged food displays to promote the consumption of fruits and vegetables. The project also generated compelling photographic and ethnographic evidence of the effects of sidewalk neglect, urban blight and lack of food shopping opportunities.

In Chicago, research into the special needs of people with disabilities, numbering nearly 600,000 city wide, led to city projects to improve sidewalks and access — part of what the study called a Health Empowerment Zone for health promotion activities. In an intervention study, the investigators studied the effects of incentives to improve mobility, food quality and physical activity on obesity.

Energized and led by NIEHS, the OBE program has operated on two-year and four/five-year grants from the NIEHS, NIH Office of Behavioral and Social Sciences Research (OBSSR), Centers for Disease Control and Prevention (CDC), National Cancer Institute (NCI) and Eunice Kennedy Shriver National Institute of Childhood Health and Human Development (NICHD). OBSSR provided financial support for the meeting enabling investigators and students to travel to and attend the meeting.

With NIEHS support now in its final year, grantees will seek support for their research from other agencies and programs. CDC representative of Amy Freeland was present to talk with individual investigators, and NIEHS Health Science Administrator Caroline Dilworth, Ph.D., made a presentation on possible opportunities for funding under the new Partnerships in Environmental Public Health Program.



CDC administrator Amy Freeland, Ph.D., was in attendance to meet investigators who may be interested in seeking CDC funding for subsequent phases of their research. (Photo courtesy of Steve McCaw)



In her report, NIEHS grantee Madeline Dalton, Ph.D., noted one study of vending machines in rural New England schools that found six out of ten offered sugar-sweetened beverages and almost one in three featured advertisements for those drinks. (Photo courtesy of Steve McCaw)



NIEHS-supported research by Principal Investigator Wenjun Li was a health geography survey intended to establish the methodological foundations for in-depth investigations and create a model for use in other urban areas throughout the country. (Photo courtesy of Steve McCaw)



Presenter John DeCastro, Ph.D., recounted the lessons of his NIEHS-funded project on the Texas-Mexico border. His team had to spend time testing and refining personal detection technologies to streamline reports of eating patterns and physical activity. Photo courtesy of Steve McCaw)



NIEHS grantee Fuzong Li was involved in several studies in Oregon that underscore an important lesson for seniors — where you live may be an important factor in determining how much of you there is. (Photo courtesy of Steve McCaw)



Division of Extramural Research and Training Management Analyst Rachel Gross, right, was one of the NIEHS employees who dropped in to hear the grantees' presentations. (Photo courtesy of Steve McCaw)

### **The Meeting's Presenters**

#### **Funded by NIEHS**

- Amy Schulz, Ph.D., and Jean Wineman, Ph.D., University of Michigan at Ann Arbor, "Lean & Green in Motown: Healthy Environments Partnership"
- Madeline Dalton, Ph.D., Dartmouth College, "Environmental and Family Influences on Adolescent Overweight and the Problem of Measuring Density in Rural Communities"
- John DeCastro, Ph.D., Sam Houston State University, "Physical Activity, Nutrition & Built Environment in a Bi-national Border Setting"
- Wenjun Li, Ph.D., University of Massachusetts Medical School Worchester "Obesity and Neighborhood Characteristics"

#### Co-funded by NIEHS and OBSSR

- Brian Saelens, Ph.D., Seattle Children's Hospital/University of Washington, "Neighborhood Impact on Kids (NIK) Project"
- Fuzhong Li, Ph.D., Oregon Research Institute, "Environmental Predictors of Elderly Obesity

#### **Funded by NICHD**

• Yochai Eisenberg, Ph.D., University of Illinois at Chicago, "Building Health Empowerment Zones for People with Disabilities"

#### **Funded by CDC**

 John MacDonald, Ph.D., RAND Corporation, "Impact of Light Rail on Physical Activity and BMI"

#### **Funded by NCI**

- Janne Boone-Heinonen, Ph.D., University of North Carolina at Chapel Hill, "Diet, Activity, Obesity & the Built Environment Dynamics"
- Natalie Colabianchi, Ph.D., University of South Carolina, "Defining the Built Environment"

## **Kindergartners Give to Two Sister Study**

By Eddy Ball

This summer NIEHS Director Linda Birnbaum, Ph.D., received a donation for the Two Sister Study from a kindergarten class at Coleytown Elementary School in Westport, Conn. It wasn't a big check by medical research standards, but the love and devotion behind the gift may make it one of the most memorable donations the study ever received.

The children in Lesa Tischler's 2008-2009 kindergarten class at Coleytown wanted to give their teacher an end-of-the-year gift. They and their parents collected a total of \$250, and Tischler requested that the money be sent in her name as a donation to the Two Sister Study directed by Principal Investigator Clare Weinberg, Ph.D., and Co-Principal Investigator Dale Sandler, Ph.D.



Funded in large part by a grant from Susan G. Komen for the Cure, the Two Sister Study was launched in 2008 as an extension of the original Sister Study. It is recruiting about 2,000 women who developed breast cancer before age 50 and are sisters of the 50,000 women already enrolled in the Sister Study.

As Weinberg explained, "This study will use a family approach to elucidate the combined roles of genes and environmental factors in causing young-onset breast cancer, and influencing the long-term prognosis and general health of women following treatment for breast cancer."

Tischler is a popular member of the Coleytown faculty. Carolyn Jumper, author of the letter to Birnbaum and one of the parents who collected the money, described her son's teacher as "truly fabulous." In a bi-monthly "On the Home Front"



Weinberg, left, and Sandler are shown in January 2008 when the Two Sister Study launched. (Photo courtesy of Steve McCaw)

column in the Westport News, Coleytown Elementary appeared as the first item of a list of reasons "Why We are Thankful to be in Westport" — with a special note of appreciation for Tischler and colleague Lori Buskey, "who give more of themselves every day than any parent could hope for."

In her thank-you note to Jumper, Weinberg said she was "moved... and also honored myself that our study was selected by you and the generous families of these young students." In closing, she promised, "We will be sure to put your donation to good use in supporting our ongoing research on young-onset breast cancer."

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## **A Stimulating Summer for Intern Amber Haynes**

By Eddy Ball

Thanks to the American Recovery and Reinvestment Act (ARRA), the 2009 NIEHS Summers of Discovery Program may prove to be a turning point for aspiring physician-scientist Amber Haynes. A graduate student with a master's degree in public health from Tulane University and a lifelong interest in science and the applications of research in clinical medicine, Haynes was clearly in her element this summer working in the NIEHS Laboratory of Respiratory Biology Environmental Cardiopulmonary Disease Group and Clinical Research Unit.

Financially, ARRA stimulus funding made possible her summer fellowship. Intellectually, her research under the supervision of NIEHS Acting Clinical Director Darryl Zeldin, M.D., and mentor Biologist Michelle Sever, who also holds a master's degree in public health, broadened her perspective on research translation. Haynes' summer internship led to a one-year appointment as a postbaccalaureate Intramural Research Training Award (IRTA) fellow for the 2009-2010 academic year.

Of her experience working in the Zeldin lab, Haynes said succinctly, "It was awesome." She added that the Summers of Discovery's integrated scientific, communications and career development program will be "very helpful" as she applies to medical schools during the upcoming year.

Looking back on some of her seminar experiences this summer, Haynes singled out the July 8 seminar "Career Options in the Biomedical Sciences." Remarks by two dual degree holders on the seminar panel — Principal Investigators Stephanie London, M.D., Dr.PH., and Carmen Williams, M.D., Ph.D. — she found especially meaningful. "Their comments encouraged me to consider obtaining a Ph.D. in Epidemiology," she said.

Haynes' work as a summer fellow culminated in her first place award in the graduate division of the summer poster competition (see related story) for her research on "Dust Mite Allergen Reduction Study: Preliminary Analysis of In-Home Test Kit Data," co-authored with Sever and Zeldin. During her year as an IRTA fellow, Haynes plans to be a presenter at several asthma meetings, including the American Academy of Allergy, Asthma and Immunology in New Orleans in February, and publish the results of her research project.

Haynes acknowledges the influence of several people and experiences in shaping her commitment to preventive medicine and translational research. In her native Atlanta, she was involved in the Medical Post Explorers Program at Morehouse School of Medicine,



"I really want to be involved in preventive medicine," Haynes said. "Working with such community groups as the Wake County Asthma Coalition is a vital contribution to preventive medicine. It is at this point that effectiveness of research is determined." (Photo courtesy of Steve McCaw)



Zeldin, above, designed the home test-kit study in collaboration with Sever and former NIEHS investigator Samuel Arbes, Ph.D. He is also supportive of Hayne's plans to pursue a doctoral degree in both medicine and epidemiology. (Photo courtesy of Steve McCaw)

and the student services coordinator there, Alex Adams, was the person who told her about NIEHS. As a graduate student at Tulane in post-Katrina New Orleans, Haynes said she gained insight into "the need for effective public health coordination during a crisis and how a lack of coordination can drastically change the quality of life of a population during and years after a disaster."

Looking ahead, Haynes reflected the ways "living and attending school in the south as an African American female afforded me a valuable perspective" on health disparities that exist in this and other demographics. "I will use [my experiences] as a guide when practicing preventive medicine," she explained. "Clinical epidemiology that involves addressing disparities in access and affordability in terms of effective health education and healthcare — not simply efficacy in intervention — is my long term interest."

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Michelle Sever, above left, "has been a wonderful mentor who generously shared her expertise in epidemiology and biochemistry," Haynes said. Sever also introduced her to people and resources at the Wake County Asthma Coalition and NIEHS. (Photo courtesy of Steve McCaw)

## **Bushel and Paules to Present at Toxicogenomics Meeting**

By Eddy Ball

NIEHS scientists Pierre Bushel, Ph.D., and Rick Paules, Ph.D., will join colleague Weida Tong, Ph.D., as U.S. representatives at the Joint Symposium of the 5th International Conference on Toxicogenomics (ICT) and 2nd Toxicogenomics Integrated Environmental Science (TIES) in Seoul, Korea September 20–23.

The conference will bring together experts in toxicogenomics from the U.S., Europe and elsewhere in Asia with their counterparts in Korea. It is sponsored by the Korean Society of Toxicogenomics and Toxicoproteomics.

Bushel, who is a staff scientist in the NIEHS Biostatistics Branch, will speak on "Delineation of Perturbed Biological Systems that Govern Hepatotoxic Potential," and Paules, principal investigator in the Environmental Stress and Cancer Group and director of the Microarrays Core Facility, will outline "An 'Omics' Approach for Identifying Biomarkers of Adverse Effects."

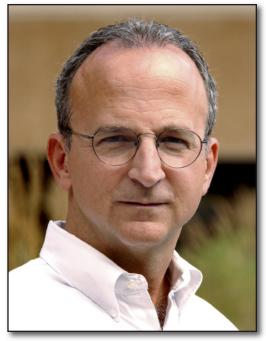


Bushel was part of the TIES organizing committee for its first meting in 2007. (Photo courtesy of Steve McCaw)

Tong will chair the meeting's Plenary Lecture I session. He is director of the Center for Toxicoinformatics at the Food and Drug Administration's National Center for Toxicological Research (NCTR) and a long-time collaborator with toxicogenomics investigators at NIEHS and the Institute's former National Center for Toxicogenomics (NCT), as well as one of the leaders of the MicroArray Quality Control Project.

The first meeting of TIES took place at North Carolina State University (NCSU) and was coordinated by NCSU Associate Director of Bioinformatics Dahlia Nielson, Ph.D., and staff in October 2007 — a year following the end of project funding by NCT. It was jointly sponsored by NIEHS, NCSU and NCTR. TIES and ICT are part of the worldwide effort to integrate high-throughput 'omics technologies and microarray platforms into toxicology and drug development.

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Paules was part of the Intramural presence in NCT. (Photo courtesy of Steve McCaw)

## **Environmental News Organization Seeks Fellowship Applications**

Environmental Health Sciences (EHS), a non-profit environmental news publisher, is accepting nominations through October 15 for ten 12-month appointments to its 2010 Science Communications Fellows program. Fellows participate in the program via a monthly conference call and one annual 2-day



meeting in Washington. Department chairs or deans at the applicant's institution make the nomination, which is accompanied by a letter from the applicant, curriculum vitae and writing samples.

The program is designed to help fellows improve their abilities to communicate with non-scientists about scientific discoveries in environmental health, especially with reporters and editors. The competition is open to postdoctoral fellows and junior faculty at research universities with active research programs in the environmental health sciences. The fellowships are part time with an annual stipend of \$5,000 and travel expenses to attend a media training conference.

Each month, the fellows identify two important new scientific findings within his or her area of expertise, compose brief summaries, and confer with colleagues and EHS staff about the findings. The fellows also contribute short reviews critiquing media coverage of environmental health findings, and occasionally, they expand the summaries into longer, more detailed synopses for the group's publications.

Environmental Health Sciences is the publisher of EnvironmentalHealthNews.org and DailyClimate.org. Nomination details and links to more information about the program and fellows from prior years — several with ties to NIEHS — are available online.

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## **Science Notebook**

## **Aging Research Yields Promising Medical Compounds**

By Robin Arnette

Harvard School of Medicine Professor David Sinclair, Ph.D., concluded the 2008-2009 NIEHS Distinguished Lecture Series on August 11 with a thought-provoking seminar titled "Pathways That Control the Pace of Aging and Disease: Prospects for New Medicines." NIEHS Principal Investigator Xiaoling Li, Ph.D., hosted the talk, which drew a capacity audience.

Sinclair is best known for his work with resveratrol, a naturally occurring molecule found in red wine grape skins and other plants. Resveratrol increases the lifespan of yeast, roundworms, flies and mice, and studies also show that rodents on high-fat diets and resveratrol are actually healthier.

The history of resveratrol begins with early studies on the association between longevity and caloric restriction (CR). Early studies demonstrated that a 30 – 40 percent daily reduction of calories slowed the aging process in rats and monkeys, so Sinclair decided to study lifespan extension in yeast as a postdoctoral fellow at M.I.T. with Leonard Guarente, Ph.D. In 1995 Guarente's lab discovered that a family of stress genes called sirtuins controlled the process of aging in yeast. Sirtuin homologues have been found in a variety of organisms, and Guarente and Sinclair believed that these genes may have evolved to help organisms survive adversity such as starvation.

The yeast sirtuin gene, *SIR2*, has a human homologue called *SIRT1*, and both protein products are deacetylases, enzymes that remove acetyl groups from target proteins in conjunction with other genes. A microarray study reported that one of the genes that was upregulated when yeast were placed under stress was *PNC1*, so Sinclair made a GFP-fusion protein with *PNC1* and determined that its activity increased under CR conditions in yeast. The experiment indicated that *PNC1* regulated *SIR2*, and both were needed for yeast to live longer. In addition PNC1-regulation of sirtuins is conserved in other organisms



Sinclair, a professor of Pathology and co-director of the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging at Harvard Medical School, said new findings in the field of aging research could usher in a revolution in medicine so that there won't just be one medicine for one disease, but one medicine for 20 diseases. (Photo courtesy of Steve McCaw)



Host Xiaoling Li, center, is head of the Mammalian Aging Group. Health Science Administrator Annette Kirshner, Ph.D., is seated in the background. (Photo courtesy of Steve McCaw)

such as the roundworm *Caenorhabitis elegans*. Sinclair noted, "The transfection of an inactive *PNC1* into *C. elegans* abolishes sirtuin activity, but if you put in extra copies of *PNC1*, it extends the lifespan compared to the wild-type worm with one copy of *PNC1*."

In 2003 Sinclair and his collaborators at Biomol International found several molecules that extended the lifespan of yeast cells in a *SIR2*-dependent manner. Sinclair called them *SIRT1*-activating molecules (STACs), and one of these STACs turned out to be resveratrol. A few years later, Sinclair wanted to see if resveratrol could mimic the benefits of CR without having to diet, so along with a collaborator at NIH, he divided up his mice into three feeding groups: mice on a lean or standard diet (SD), mice on a high-fat diet, also called the Western diet, and mice on a Western diet plus resveratrol.

At 15 months the SD mice were lean, while the Western diet mice and the Western diet plus resveratrol mice were obese. However, the resveratrol mice were physiologically different. "Looking at the resveratrol mice, there's no way they could live longer or be healthier or run further, but that is exactly what we found," Sinclair explained. "Even pathologists who were studying the tissue samples couldn't tell the difference between the resveratrol and SD mice."

Harvard University and Sinclair co-founded a company called Sirtris that is developing synthetic STACs for humans. The drug is well-tolerated, seemingly safe and in early clinical trials lowered blood glucose levels and improved insulin sensitivity in diabetic patients. Sirtris, now owned by GlaxoSmithKline, has designed new chemical molecules that are up to a 1000 times more potent than resveratrol. In three different diabetes models, these drugs reduced glucose and cholesterol levels and were highly anti-inflammatory.



The diverse audience included National Toxicology Program scientists Jef French, Ph.D., center, and Lori White, Ph.D., seated to the right. (Photo courtesy of Steve McCaw)



NIEHS Clinical Research Center Medical Director Stavros Garantziotis, M.D., was interested in the therapeutic implications of Sinclair's findings and the clinical trials now underway. (Photo courtesy of Steve McCaw)

Li, who described Sinclair as "the inspiration for my own research," has also been investigating the role of *SIRT1* in lipid metabolism and inflammation. She says that Sinclair's observations are in line with her recent findings that deletion of hepatic *SIRT1* results in hepatic steatosis or fat buildup and inflammation.

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## **Summer Students Explore Basics of Epidemiology**

By Laura Hall

In the last interactive Summers of Discovery seminar of the year on August 5, NIEHS Epidemiology Branch Chief Dale Sandler, Ph.D., and Senior Investigator Allen Wilcox, M.D., Ph.D., worked as a team to give the students "a taste of epidemiology." With their team approach and small group discussion format, the duo kept the pace varied and the students engaged.

Wilcox opened the seminar by telling the audience that they would explore "how in a broad sense epidemiology can be applied to environmental questions" and learn about the "nuts and bolts aspects" of how epidemiologists make observations from their studies. Pointing out that epidemiology is an observational science, Wilcox told the students that epidemiological observations can be hard to interpret because scientists cannot control the conditions as they do in experimental science. Epidemiology studies can establish associations, but researchers must always keep in mind that there could be alternate explanations for the results.

Sandler explained that epidemiologists study populations not individual patients or cells. Epidemiologic studies are not necessarily about mechanisms, although some studies do lead to insights about mechanisms or test, in the real world, theories that derive from mechanistic studies. Sometimes, epidemiology studies can show that environmental health problems exist before any mechanism is known, she noted. As part of the discussion, the students mentioned some of the environmental agents causing health

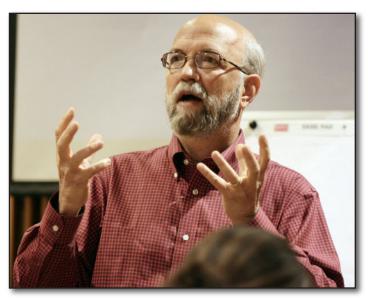
problems that they recognized, such as asbestos, endocrine disruptors, tobacco smoke, drinking water pollutants and pesticides.

Sandler continued with an historical perspective on pesticide use and how awareness of deleterious health effects gradually developed. She talked about the Agricultural Health Study (AHS) she is presently involved with here at NIEHS. The AHS is a study of licensed pesticide applicators and their spouses and is the largest study of farmers in the world.

In explaining why epidemiologists wanted to study the effects of pesticide use on farmers, Sandler told the students, "You and I have no clue what amount and what kind of pesticide we're exposed to." She stated that it is much easier to study health effects of pesticides or other chemicals in workers rather than in the general population.



Summer intern Bryce Schroeder listened intently as Wiilcox described the work of epidemiologists on environmental health hazards. (Photo courtesy of Steve McCaw)



Wilcox said that an epidemiologist's study design is like Galileo's telescope — it must be carefully created to study patterns in data. (Photo courtesy of Steve McCaw)

For farmers, it is possible to collect extensive data on pesticide exposures and work practices. Since farmers apply pesticides only some days of the year, their overall exposures are more similar to general population exposures than if they were handling chemicals every day. Their family members have potential exposures even when they are not engaged in farming.

Using the AHS as an example, Sandler discussed the types of epidemiology studies that can be performed, such as mortality, case-control and cohort studies. She observed that epidemiology studies can take a long time, particularly when the outcome of interest is a rare disease. Political and economic forces can contribute to resistance to acknowledging a health hazard indicated by epidemiology studies.

After this overview, the audience divided into two groups led by Sandler and Wilcox to discuss a recent news report that the Navajo population living near formerly active uranium mines are concerned about possible health effects caused by radiation exposure. Lung cancer and other lung diseases are a well-established consequence of uranium mining but health effects among persons who do not work in the mines have not been established. The goal was to determine what factors should be considered in designing an epidemiology study on this case.

The students came up with ideas about what kind of information could be gathered, how to identify exposed people and route of exposure, and how to find comparison controls that are unexposed or have lower levels of exposure. Group members talked about ethical issues and the need to consider cultural issues when recruiting potential study participants. They also pondered how to document health outcomes

In all, the students came away with a fresh and more detailed understanding of the value of epidemiology and the factors that must be considered when designing and interpreting the studies.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)

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Sandler told the students, "One of the fundamental things and the hardest things that epidemiologists have to work on is thinking about ruling out alternate explanations." (Photo courtesy of Steve McCaw)



Wilcox listened as students discussed designing an epidemiology study on the Navajo uranium mining case example. (Photo courtesy of Steve McCaw)



Sandler, center background, discussed the example case with one group of students (Photo courtesy of Steve McCaw)

## **Superfund Study of Carbon Nanoparticle Toxicity in Adult Flies**

By Rebecca Wilson

Researchers at Brown University's NIEHS-funded Superfund Research Program (Brown SRP) report in the latest edition of *Environmental Science and Technology* that carbon nanoparticles cause a significantly higher mortality rate in adult fruit flies than in very young flies. This finding was observed in a series of experiments conducted on larval and adult *Drosophila* fruit flies using several types of carbon nanoparticles commonly found in medicine, electronics and office settings.

According to the authors, the findings are important because they show that permutations of the same material can have different effects in the environment. "It's not the nanoparticle per se that may be hazardous," said corresponding author David Rand, Ph.D., "but the form the particle is in."

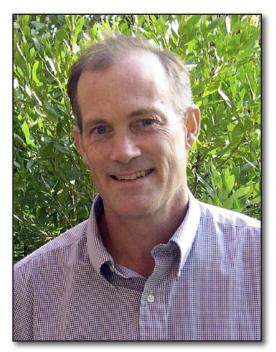
In the experiments, Rand, Robert Hurt, Ph.D., and other Brown SRP researchers exposed *Drosophila* larvae to one of four types of carbon nanoparticles, carefully blending it into their food so the larvae could not detect it or choose to avoid eating it. The larvae seemed to have no physical or reproductive effects from consuming the nanoparticles, though some of the nanoparticles appeared to be incorporated in the larvae, where they remained through maturation and showed in adult tissue. This could indicate that, with the proper conditions, bioaccumulation to larger animals might occur in nature.

The adult flies weren't so lucky. They were sealed into a test tube that contained a dry sample of the particles, and the test tube was taped, causing the flies to fall into the powdery particles. At that point, the investigators used a timer to determine how long it took the exposed flies to climb back to the top of the test tube. Flies exposed to carbon black and single-walled nanotubes were engulfed in the fine dust and, unable to remove it, died within a few hours. Other materials did not cover the flies so thoroughly, and they were able to remove the particles through normal grooming mechanisms.

Though the exact mechanism of toxicity is unclear, analysis by lead author Xinyuan Liu, a Ph.D. student in chemistry at Brown funded by the SRP, revealed several possibilities. Some flies were covered



First author Xinyuan Liu. (Photo courtesy of Xinyuan Liu)



Corresponding author David Rand. (Photo courtesy of Brown University)

in dust from head to toe, including their wings, which could have impeded their movement. Still others might have been blinded by the particles covering their eyes or suffocated from particles clogging their spiracles, or breathing holes. "It's like a dinosaur falling into a tar pit," commented Rand. "[The particles] glom onto the flies. They just can't move."

A related experiment was conducted concurrently with those published in *Environmental Science & Technology*. In this experiment, led by undergraduate student Daniel Vinson, adult *Drosophila* were covered in nanoparticles and then allowed to walk from one test tube to another, depositing particles along the way. The transport caused clean, control flies to be contaminated with some of the nanoparticles. This experiment demonstrated how insects could be vectors for transporting nanomaterials and other materials, such as bacteria or intestinal parasites.

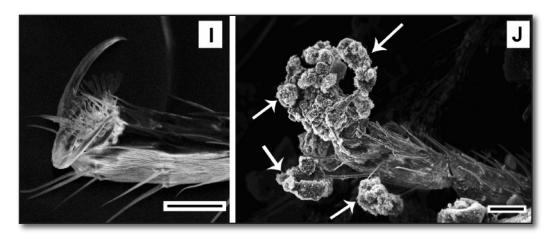
Several related experiments are planned. The researchers intend to determine the cause of death for the flies that were exposed to carbon black and single-walled nanotubes, and investigate the differences between the nanoparticles that led them to cause death in some flies but not others. In addition, the researchers intend to investigate the effects other nanoparticles, such as nanosilver, have on *Drosophila*.

Citation: Liu X, Vinson D, Abt D, Hurt RH, Rand DM. 2009. Differential Toxicity of Carbon Nanomaterials in Drosophila: Larval Dietary Uptake Is Benign, but Adult Exposure Causes Locomotor Impairment and Mortality. Environ Sci Technol 43(16):6357–6363. Epub ahead of print. DOI: 10.1021/es901079z

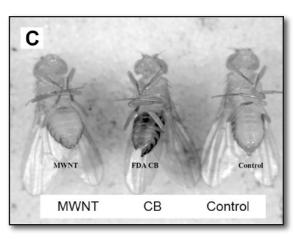


Hurt heads the Laboratory for Environmental and Health Nanoscience at Brown. He and his group have published extensively on nanomaterials and environmental health. (Photo courtesy of Brown University)

(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)



Drosophila leg and foot are shown unexposed (I). After spherical aggregates exposure (J), multiwalled nanotubes (MWNT) adhere to the Drosophila pincer structure used for gripping (see arrows). Scale bars equal 20 micrometers or millionths of a meter (µm). (Photo courtesy of Robert Hurt and Brown University)



Adult Drosophila hatched from carbon nanomaterial-containing food, left and center, have sequestered particles in tissues associated with external bristles or darkened abdominal regions. Compared to the unexposed control, right, the effects are the most evident in the carbon black (CB) sample. (Photo courtesy of Robert Hurt and Brown University)

## **Epigenetic Changes Associated with Prenatal Tobacco Exposure**

By Negin Martin

A new NIEHS-funded study published by researchers at the University of Southern California (USC) reports that life-long effects of prenatal exposure to tobacco may be mediated by changes in DNA methylation.

The USC study, soon to be published in the *American Journal of Respiratory and Critical Care Medicine* and now online, provides some of the first evidence that alterations in the epigenome may be a possible mechanism for life-long and even inherited effects of *in utero* exposure to tobacco smoke. This is the first study to report changes in DNA-methylation in cells from the oral cavity after prenatal exposure.

"This research could be an important first step into understanding how we may be able to intervene in these developments on an epigenetic level," said first author Carrie Breton, Sc.D. "This research could also lead to new ways for researchers to investigate biological mechanisms that might explain known health effects associated with maternal smoking."

Prenatal exposure to tobacco smoke has been linked to increased incidence of asthma and pulmonary disease in children. However, it is poorly understood why the adverse health effects associated with maternal smoking persist through children's lives and are in some cases transgenerational.



First author Carrie Breton is currently an assistant professor in the USC Department of Preventive Medicine and a collaborator in the Children's Environmental Health Science Center at the University of Southern California. (Photo courtesy of Carrie Breton)

The study's lead investigator, Frank Gilliland, M.D., Ph.D., is a Professor of Preventive Medicine and the Director of the Division of Environmental Health at the University of Southern California in Los Angeles. Gilliland's research focuses on genetic and dietary factors that contribute to environmentally triggered lung disease and breast cancer. As a principal investigator, he has published a number of epidemiological studies about the effects of radon exposure on progeny and the adverse respiratory effects of air pollution.

Gilliland's team of scientists discovered gene-specific and global alterations in DNA methylation patterns of children who were exposed to tobacco smoke *in utero*.

The researchers collected buccal cell samples from over 300 kindergartners and first graders to look for global DNA methylation patterns. Buccal cells – pronounced "buckle" – are aero-digestive cells that are constantly regenerated and shed. These cells can be collected by gently scraping the inside of the cheek and can be used for genetic studies. A questionnaire was used to determine the maternal smoking history.

Two DNA repetitive elements, long interspersed nucleotide element 1 (LINE1) and short interspersed nucleotide element (AluYb8), served as surrogate markers for the detection of global methylation. AluYb8 methylation was significantly lowered in exposed children. No significant differences between LINE1 methylation of exposed and unexposed children was evident unless children carried a mutation in their Glutathione S-transferase Mu1 (GSTM1) genes.

GSTM1 is a detoxifying enzyme that protects the body against carcinogens, oxidative stress and environmental toxins. Silencing mutations in GSTM1 increase susceptibility to adverse health effects of smoking. Exposed children with GSTM1 null mutation showed differences in their LINE1 methylation pattern.

The results of this study suggest that maternal smoking during pregnancy and GSTM1 gene variations are contributing factors to epigenetic changes in exposed children.

Epigenetic changes can persist through multiple cell divisions, cell differentiation and even be passed on to progeny. Unlike DNA mutations, epigenetic changes are reversible since the sequence of DNA remains unaltered. Long-term effects of many environmental pollutants including tobacco smoke are suspected to be mediated through epigenetic changes to DNA.

Currently, there are over a billion tobacco users worldwide. Smoking tobacco claims over 5 million lives annually and is the number one preventable cause of death in the world.

Citation: Breton CV, Byun HM, Wenten M, Pan F, Yang A and Gilliland FD. 2009. Prenatal Tobacco Smoke Exposure Affects Global and Gene-Specific DNA Methylation. *Am J Respir Crit Care Med.* Epub ahead of print.



Gilliland, shown at a 2008 meeting in Chapel Hill, is the principal investigator on three NIEHS grants, which are associated with more than 300 publications. In addition to NIEHS funding, support for this study was provided by the Hastings Foundation and the American Society of Clinical Oncology. (Photo courtesy of Steve McCaw)

(Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core Facility and a 2009 Science Communication Fellow with Environmental Health Sciences. She recently completed a postdoctoral fellowship with the NIEHS Membrane Signaling Group.)

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# Research Suggests Viral Protein Manipulates Host Cells to Cause Flu-like Symptoms

By Brian Chorley

In response to the current H1N1 pandemic, the scientific community has increased its efforts to better understand how influenza virus spreads and how to mediate its adverse health effects. Physiologist Sadis Matalon, Ph.D., of the University of Alabama in Birmingham (UAB), and an NIEHS-supported research group, which included influenza experts Diana Noah, Ph.D., and James Noah, Ph.D., of the Southern Research Institute Emerging Infectious Diseases section in Birmingham, are currently exploring such issues by determining the mechanisms by which influenza virus invades its host and propagates.

In their recent study, available online from the *Journal of the Federation of American Societies for Experimental Biology (FASEB)*, Matalon and his research team demonstrated for the first time how a specific viral protein, M2, decreases airway cell ion channel activity, which can lead to flu symptoms such as pulmonary edema. Understanding this mechanism may lead to "new therapeutic strategies for altering the progression of the viral infection" and for maintaining alveolar fluid absorption, the authors conclude.

According to the researchers, influenza is a highly contagious respiratory virus responsible for an estimated 36,000 deaths annually in the U.S. alone. It infects humans and other animal species, such as dogs, horses, pigs and birds. The virus is highly adaptable to its environment because of its ability to incorporate genetic material from different viral strains, thereby creating a novel strain not recognized by the immune system of the host. For example, the current H1N1 strain evolved from strains that previously infected humans, birds and swine.

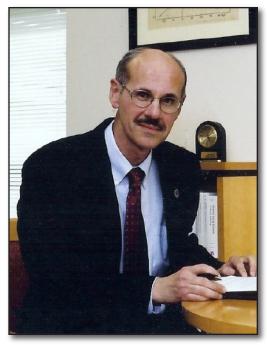
Understanding the mechanisms by which influenza viruses evolve, invade and replicate also clues scientists as to why viruses create flu-associated symptoms. Many of the respiratory symptoms can be attributed to signaling changes mediated by the airway epithelial cells. The virus first encounters this cellular lining, which protects the airway from environmental challenges. These cells were the focus of Matalon's study.

Specifically, changes in sodium transport across the epithelial cell lining after influenza virus exposure was measured. Sodium transport directly influences the absorption of fluid that lines the trachea and distal airways. Abnormal buildup of this fluid, or pulmonary edema, reduces the ability of oxygen exchange in the lung, which can be fatal. In the study, the researchers demonstrated that the M2 protein attenuates the presence of the epithelial sodium transport channel ENaC.

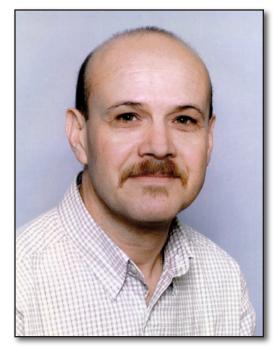
M2 protein itself is an ion (proton) channel and is utilized by the virus to create an environment conducive for replication. Since M2 protein functions in the same cellular space as ENaC, the research team looked for interaction between the two ion channel proteins that could explain M2-mediated regulation of ENaC. Surprisingly, they found that M2 increased targeted degradation of ENaC through an indirect mechanism involving reactive oxygen species production and a downstream protein kinase cascade.

Decreased amounts of active ENaC through the action of viral M2 protein may contribute to fluid buildup in the airway. This buildup could lead to pulmonary edema, as well as contribute to less serious flu symptoms, such as runny nose. Medications that specifically target the viral M2 protein, such as amantadine, should act to dampen these symptoms by inhibiting ENaC depletion.

Unfortunately, due to their highly adaptable nature, many viral strains are amantadine-resistant, limiting the effectiveness of this medication as an anti-viral treatment. Evidence provided by this study demonstrates, however, that targeting M2 protein may have multiple beneficial effects. Perhaps findings such as these will lead to future efforts to develop novel drug therapy that targets the viral M2 channel.



Matalon, above, credited the recently established Pulmonary Injury and Repair Center at UAB for making possible "an effective collaboration among physiologists and cell biologists from the University of Alabama at Birmingham and virologists from the Southern Research Institute to help address a significant health problem." (Photo courtesy of Sadis Matalon)



First author Ahmed Lazrak, Ph.D., is a research associate and colleague of Matalon in the Department of Anesthesiology, one of four departments of the UAB Schools of Medicine and Public Health that contributed expertise to this trans-disciplinary effort. (Photo courtesy of Sadis Matalon)

The study was supported by grants from multiple institutes of the National Institutes of Health, including the National Institute of Environmental Health Sciences. The findings will be published in the November 2009 edition of *FASEB*.

Citation: Lazrak A, Iles KE, Liu G, Noah DL, Noah JW, Matalon S. 2009. Influenza virus M2 protein inhibits epithelial sodium channels by increasing reactive oxygen species. FASEB J. [Epub ahead of print]

(Brian Chorley, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

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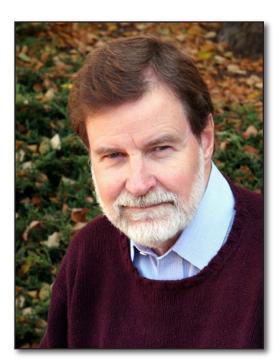
## Wilson Chairs Gordon Conference on Genetic Toxicology

By Eddy Ball

NIEHS Laboratory of Structural Biology (LSB) Principal Investigator Samuel Wilson, M.D., served as the chair of the 2009 Gordon Conference on Genetic Toxicology August 9–14 at Colby-Sawyer College in New London, NH. Among the approximately 150 attendees were several NIEHS intramural scientists and grantees who made presentations, along with other specialists in public sector and private sector research. More than 25 percent of posters entered into competition represented the work of NIEHS-supported investigators.

Genetic toxicology is an interdisciplinary endeavor that combines investigations into structural, molecular and cellular biology, genetics, biochemistry, epidemiology, toxicology, adverse drug reactions, toxicogenomics and hazard assessment. The program was divided into four areas of investigation — Environmental and Endogenous Genotoxic Stress, Mutagenesis and Lesion By-Pass, Chromatin and Links to Genotoxicity, and DNA Damage and Cellular Decisions.

Presentations by NIEHS intramural scientists reflected the broad range of research interests reported during the meeting. LSB Chief Tom Kunkel, Ph.D., explored "Efficiency of repairing polymerase- and strand-specific DNA replication errors." Laboratory of Molecular Genetics (LMG) Principal Investigator Mike Resnick, Ph.D., addressed "The expanding p53 universe of target genes," and



Chair Sam Wilson is the latest of a series of NIEHS scientists who have chaired the Gordon Conferences on Genetic Toxicology since their inception nearly 30 years ago. (Photo courtesy of Steve McCaw)

his colleague, Staff Scientist Dmitry Gordenin, Ph.D., spoke on "Damage-induced localized hypermutability." Former LMG Principal Investigator Ben Van Houten, Ph.D., who is now at the University of Pittsburgh, discussed "Reactive oxygen species an genotoxic stress."

Notable NIEHS grantees included Director of the Columbia Center for Children's Environmental Health Frederica Perera, Dr.P.H., and Massachusetts Institute of Technology Professor and Director of the Center for Environmental Health Sciences Leona Samson, Ph.D. Perera described recent work with a cohort of mothers and infants in New York, "Effect of prenatal environmental exposures on the genome and epigenome." Samson focused on the inflammatory cascade linked to cancer in "Complex response to alkylating agents."

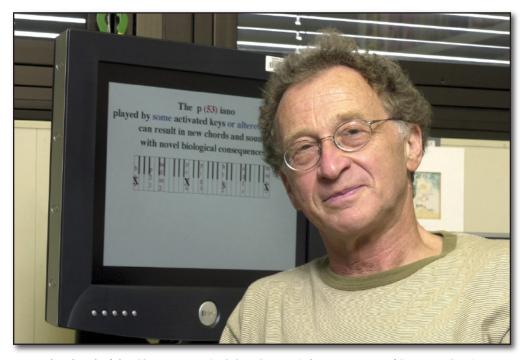
The biannual Gordon Conference on Genotoxicology was first convened in 1981. The meetings provide an international forum for the presentation and discussion of pioneering research in the biological, chemical, and physical sciences, as well as their related technologies.



In addition to serving as chief of LSB, Kunkel holds an appointment in LMG as head of the DNA Replication Fidelity Group. (Photo courtesy of Steve McCaw).



Gordenin and Resnick collaborate frequently on studies of DNA strand break repair. (Photo courtesy of Steve McCaw)



Resnick is head of the Chromosome Stability Group. (Photo courtesy of Steve McCaw)

## **An NTP Caveat — Predictive Toxicity and Nanomaterials**

By Eddy Ball

In a forum series article published in the August issue of *Toxicological Sciences*, National Toxicology Program (NTP)
Deputy Program Director for Science Nigel Walker, Ph.D., and NTP Associate Director John Bucher, Ph.D., take a critical look at the 21st century paradigm for evaluating the health hazards of nanoscale materials. Walker and Bucher explore the strengths and weaknesses of applying high-throughput predictive toxicity strategies to assessment of the potential health risks of the proliferating number and types of nanomaterials now in use or currently in development.

NTP and other organizations are involved in proactive efforts to move toxicology from a predominantly observational science to a predominately predictive one by integrating new high-throughput screening (HTS) technologies. As outlined in the National Research Council (NRC) report "Toxicity Testing in the 21st Century," HTS may be key to developing predictive models for anticipating *in vivo* biological responses to chemical exposures. Recently, several predictive methodologies have been proposed for applying the NRC paradigm to studies of existing and emerging nanoscale materials.

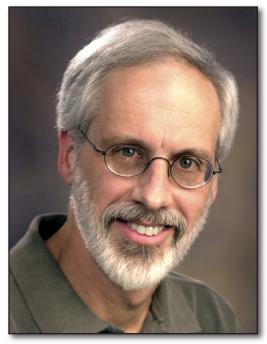
In their paper, the authors concede, "It is clear that a one-by-one approach to toxicity testing [of nanoscale materials] is not a tenable strategy." However, they also argue that, unlike chemicals and other simpler substances, nanoscale materials present new and different challenges for assessment because of their various sizes and shapes, differing composition from manufacturer to manufacturer, engineering and sometimes unpredictable behaviors, such as agglomeration and aggregation — all of which contribute to making chemical characterization and determination of dosimetry "an area that requires significantly more attention [in HTS screening] than would be paid to most chemicals."

Along with these factors, the testing environment itself may create special issues for determining what is "purity" for a nanomaterial in the assessment of its appropriate physicochemical properties. "The specific composition of an *in vitro* and *in vivo* test system will likely play a huge role in how a nanomaterial interacts with a cell or other biological target," Walker and Bucher contend. "What was 'tested' may often bear little resemblance to the material as it exists in the real world or in a different test system."

While Walker and Bucher admit that some nanomaterials may offer "a tailor-made test case" for the new paradigm, they suggest that "the healthy debate among toxicologists, regulators and the public at large" over this issue will continue. With so much still to be understood about nanoscale materials, the authors warn, "by virtue



Walker has been the NTP lead on the potential health risks posed by exposure to nanoscale materials in the environment. (Photo courtesy of Steve McCaw)



Bucher, who assumed leadership of NTP in 2007, is guiding the organization as it evolves to meet the needs of toxicology in the 21st century. (Photo courtesy of Steve McCaw)

of their physical attributes and unpredictable and/or artifactual behavior in *in vitro* systems, the majority of nanomaterials may not be amendable to study in high throughput assays."

*Citation:* Walker NJ, Bucher JR. 2009. A 21st century paradigm for evaluating the health hazards of nanoscale materials? Toxicol Sci 110(2):251-4. [Epub before print]

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#### This Month in EHP

By Eddy Ball

The August issue of Environmental Health Perspectives (EHP) highlights H1N1 influenza with a Focus article on the possible role of concentrated animal feeding operations (CAFOs). It presents an analysis of arguments for and against this unproven but biologically plausible hypothesis.

A Spheres of Influence article explores efforts by the "new" United States Department of Agriculture under the leadership of Secretary Tom Vilsack to revamp the agency's role as the nation's food steward and to promote improved public and environmental health.

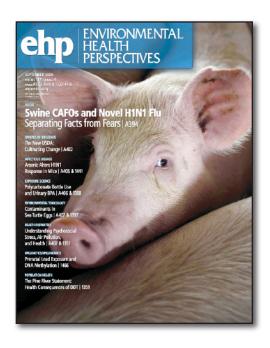
A new study reports on dramatic evidence that chronic arsenic (As) exposure increases the effects of H1N2 exposure in mice and hypothesizes that exposure to As-contaminated drinking water might have similar effects in human populations.

Highlights from the issue include the following studies:

• Polycarbonate Bottle Use and Urinary BPA — Compares BPA levels in 77 college students who used stainless steel container for one week to levels in the same students after using polycarbonate plastic drinking bottles for a week. The investigators found that BPA concentrations increased 69 percent on average after use of the polycarbonate bottles.



http://twitter.com/ehponline



- Contaminants in Sea Turtle Eggs Investigates levels of persistent organic pollutants in green turtle eggs sold for human consumption from local markets in Peninsular Malaysia. The researchers reported levels of coplanar PCBs at more than 300 times the accepted daily intake and levels of arsenic and selenium high enough to affect developmental and reproductive outcomes in sea turtles.
- Understanding Psychosocial Stress, Air Pollution, and Health Reviews research on the potentially synergistic effects of exposure to high levels of both pollution and psychosocial stress on health, calling for additional experimental and observational studies to better understand the interplay of environmental and psycho-social factors.

## **Birnbaum To Give Distinguished Lecture September 8**

By Eddy Ball

NIEHS opens its 2009–2010 Distinguish Lecture Series on September 8 with a talk on "Halogenated Flame Retardants: Does the Benefit Justify the Risks?" by NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D. The lecture will begin at 11:00 in Rodbell Auditorium, hosted by the NIEHS Women's Science Assembly and NTP Toxicologist Michelle Hooth, Ph.D.

Birnbaum is a recognized leader in research on halogenated flame retardants. She delivered a plenary lecture at the 11th Annual Workshop on Brominated Flame Retardants (BFR2009) held May 19–20 at the Government Conference Centre in Ottawa. In August, she taught a course on the topic in China. She has authored more than 300 papers published in peer-reviewed journals.

Her talk will explore innovative research on various aspects of exposure to the various synthetic compounds used as flame retardants. Her talk will balance the benefits and health risks of these ubiquitous and persistent chemicals, especially in terms of early exposures leading to later diseases, present an update on measures to ban compounds by governments worldwide, and offer a critical look at the alternatives now in use or proposed for future applications to inhibit the spread of fire.



NIEHS Director Linda Birnbaum (Photo courtesy of Steve McCaw)

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## **Extramural Update**

#### **Small Business Innovation Research (SBIR) Contract Solicitation**

As part of its Small Business Innovation Research (SBIR) program, on August 17 the National Institutes of Health (NIH) in conjunction with the Centers for Disease Control and Prevention (CDC) published a Request for Proposals (RFP) SBIR Contract Solicitation in the Federal Register.

The NIH is accepting proposals from small business concerns with the research and development (R&D) expertise to conduct innovative research that will contribute toward meeting the program objectives of the agencies. The complete announcement may be found online. The date of receipt for all proposals is November 9, 2009.

The NIEHS SBIR program is integrated into the overall research agenda of NIEHS with the goal of developing and commercializing technologies and products in the area of environmental health sciences that will reduce the burden of human illness and dysfunction from environmental causes. The NIEHS program consists of both grant and contract opportunities. The NIEHS grants program, part of the NIH omnibus solicitation will be announced in January for 2010.

The NIEHS is currently seeking contract proposals that address the following needs:

- Computer Assisted Sperm Analysis System
- Development of Quantitative High-Throughput Screens For Environmental Toxicants that Induce DNA Damage
- Development of Mid- to High-Throughput Toxicological Tests Using Model Organisms Integrated Prediction Systems to Support Environmental Toxicological Assessments
- Incorporation of Metabolism into Quantitative High-Throughput Screening (HTS) Assays
- Development of Quantitative High-Throughput Screens for the Detection of Chemicals That Modulate Gap Junctional Intercellular Communication
- Monitoring in vivo Gene Expression Changes After Exposure to Toxicants in Caenorhabditis elegans
- Development of Biomarkers for Assessment of Exposure to Molds

The SBIR program is a set-aside program for small business concerns to engage in Federal research and development with the potential for commercialization. This program was developed in 1992 to stimulate technological innovation, foster and encourage participation by minorities and disadvantaged persons in technological innovation, and to increase private-sector commercialization of innovations derived from Federally funded research, e.g. to translate basic science discoveries into commercial products.

The NIEHS SBIR program is part of the NIH/DHHS program and details including receipt dates, forms, program announcements and grantsmanship guidance can be found on the NIH SBIR website.

The NIEHS contact is Jerry Heindel, Ph.D.

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Health Science Administrator Jerry Heindel oversees NIEHS grants in the Small Business Innovative Research and Small Business Technology Transfer programs. (Photo courtesy of Steve McCaw)

#### **Extramural Papers of the Month**

By Jerry Phelps

- · "Sloppier Copier" Mysteries Solved
- Bisphenol A Reduces the Effectiveness of Chemotherapeutics
- Progesterone Triggers Breast Inflammation
- Potential Discovery of New Asthma Therapy



Read the current Superfund Research Program Research Brief. New issues are published on the first Wednesday of each month.

#### "Sloppier Copier" Mysteries Solved

New discoveries by NIEHS-funded biologists solved a vexing question about the role of the protein RecA in DNA repair and determined the exact composition of the active form of the DNA repair enzyme polymerase V.

RecA is a nucleoprotein filament, which is a long line of proteins bound to a single-stranded DNA. It transfers two molecules to polymerase V resulting in the enzymes activation — ATP for fuel and a single RecA protein. Although RecA does not actively participate in the repair process, it activates polymerase V, which as a result begins walking down the damaged DNA segment copying a new strand. As soon as it reaches the end of the damaged section, it drops off the DNA and immediately deactivates. It must be reactivated by RecA to copy more DNA, in contrast to all other DNA polymerases.

In 1999, researchers in this laboratory discovered polymerase V, which was nicknamed the "sloppier copier" because it makes frequent copying mistakes that show up as mutations in the cell's DNA. The researchers postulate that polymerase V may be more important for the long-term success of a species than its more accurate counterparts because some of the mutations are likely to be helpful, enabling organisms to better adapt to their environments.

Citation: Jiang Q, Karata K, Woodgate R, Cox MM, Goodman MF. 2009. The active form of DNA polymerase V is UmuD'2C-RecA-ATP. Nature 460(7253):359-363.

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#### **Bisphenol A Reduces the Effectiveness of Chemotherapeutics**

Recent research results suggest that the environmental estrogen bisphenol A (BPA), in addition to its potential carcinogenic and reproductive health effects, reduces the effectiveness of three common chemotherapeutic agents used to treat breast cancer.

BPA is structurally similar to diethylstilbestrol (DES) and its carcinogenic potential is of strong concern to scientists and regulators. Similar to DES, BPA has estrogenic activity, and exposure in young rodents leads to increased rates of hormonally related cancers as the animals age. Since estrogen has been shown to antagonize some anticancer drugs, the research team wanted to test BPA for its potential to reduce the effectiveness of these anticancer agents.

The findings were clear. At nanomolar concentrations of BPA, levels routinely found in humans, estrogen receptor-positive and –negative breast cancer cells lines were protected from the chemotherapeutic effects of doxorubicin, cisplatin, and vinblastine. The researchers speculate that the protective effect could be the result of increased expression of anti-apoptotic proteins caused by BPA.

This study highlights a previously unrecognized effect of BPA in carcinogenicity and therefore adds strong support to the growing knowledge of the adverse effects of BPA on human health. It also suggests that BPA exposure may be a factor in choosing therapeutic regimens in patients undergoing treatment for hormonally related cancers.

*Citation:* Lapensee EW, Tuttle TR, Fox SR, Ben-Jonathan N. 2009. Bisphenol A at low nanomolar doses confers chemoresistance in estrogen receptor-alpha-positive and –negative breast caner cells. Environ Health Perspect 117(2):175-180.

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#### **Progesterone Triggers Breast Inflammation**

NIEHS-funded researchers at Michigan State University report that exposure to the hormone progesterone activates genes that trigger inflammation in the mammary gland. This inflammation may be a key factor in increasing the risk of breast cancer.

Paradoxically, progesterone promotes normal development of the breast, but it has been previously identified as a risk factor for breast cancer. Exposure to progesterone in normal amounts causes breast inflammation, which leads to development. However, exposure to progesterone in post-menopausal hormone therapy is a known risk factor for breast cancer.

In a laboratory mouse study, the researchers examined genes activated by progesterone and the effects of their activation. They found that progesterone regulates 162 genes in pubertal cells, 104 genes in adult cells and 68 genes in cells during both developmental stages. Some of these genes code for small proteins called chemokines that are active in the process of inflammation.

The study identified the targets of progesterone receptor A in mammary cell development. These links provide avenues of research and potential therapies in reducing the influence progesterone has on developing breast cancer.

*Citation:* Santos SJ, Aupperlee MD, Xie J, Durairaj S, Miksicek R, Conrad SE, Leipprandt JR, Tan YS, Schwartz RC, Haslam SZ. 2009. Progesterone receptor A-regulated gene expression in mammary organoid cultures. J Steroid Biochem Mol Biol 115(3-5):161-172.

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#### **Potential Discovery of New Asthma Therapy**

NIEHS-funded clinical investigators discovered that a single enzyme is critical in most allergen-induced asthma attacks. The activity of the enzyme, aldose reductase, can be significantly reduced by drugs that have already undergone clinical trials for diabetes complications.

In a wide variety of diseases, including cancer, atherosclerosis, asthma and diabetes, exposure to high levels of reactive oxygen species (ROS) leads to the release of a barrage of inflammatory signaling proteins. These proteins stimulate more immune system cells to enter the affected tissue causing the release of even more ROS, producing a cycle of ever-increasing inflammation.

Aldose reductase plays a pivotal role in the activation of inflammatory processes. Knowing that asthma is a chronic disease of inflammation, the research team postulated that aldose reductase inhibition would have beneficial effects in preventing asthma exacerbations.

Experiments were carried out in cultures of human airway epithelial cells. Compared to untreated cells, cells treated with an enzyme inhibitor had a much milder inflammatory response to ragweed pollen exposure. Similar studies in live mice also showed that mice given an aldose reductase inhibitor had a dramatically reduced inflammatory response after exposure to ragweed pollen.

The research team plans to conduct clinical trials to determine whether aldose reductase inhibitors will be beneficial in treating human asthma.

Citation: Yadav UC, Ramana KV, Aguilera-Aguirre L, Boldogh I, Boulares HA, Srivastava SK. 2009. Inhibition of aldose reductase prevents experimental allergic airway inflammation in mice. PLoS One 4(8):e6535.

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training. Each month, he contributes summaries of extramural papers to the *Environmental Factor*.)

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### **Intramural Papers of the Month**

By Robin Arnette and Laura Hall

- RAP80, Part of an Autoregulatory Loop with HDM2 and p53, Enhances p53 Degradation
- Alpers Disease Mutations In Polymerase Gamma Impair Mitochondrial DNA Replication
- Mi-2/NuRD Is Part of a Novel Chromatin Assembly Pathway
- Web-Based SNP Tools Offer Unique Usability Features

# RAP80, Part of an Autoregulatory Loop with HDM2 and p53, Enhances p53 Degradation

NIEHS researchers have discovered a new role for receptor-associated protein 80 (RAP80) as a mediator of E3 ubiquitin ligase HDM2 (HDM2) ubiquitination of p53 and as a direct transcriptional target of p53 following DNA damage.

RAP80 together with HDM2 and p53 form an autoregulatory loop. Higher RAP80 levels lead to destabilization of p53, making blocking of the p53-RAP80 interaction a possible therapeutic strategy against human cancers with low p53 expression.

The transcriptional factor p53 is a master regulator in DNA damage, cell cycle control and cell death. It is involved in preventing cancer by functioning as a tumor suppressor. The physiological level of p53 is normally kept low through ubiquitination by HDM2 and then degradation by the proteosome. p53 can activate the transcription of *HDM2* gene, initiating p53 destabilization and creating an autoregulatory loop.

*RAP80* gene was shown to also be a direct transcriptional target of p53 through a noncanonical response element in *RAP80*. The p53 DNA-binding domain bound RAP80. The effect of RAP80 on p53 ubiquitination was dependent on HDM2 expression — the ubiquitin interaction motifs of RAP80 were not involved.

Citation: Yan J, Menendez D, Yang X-P, Resnick M, Jetten AM. 2009. A regulatory loop composed of RAP80-HDM2-p53 provides RAP80-enhanced p53 degradation by HDM2 in response to DNA damage. J Biol Chem 284(29):19280-19289.

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# Alpers Disease Mutations In Polymerase Gamma Impair Mitochondrial DNA Replication

Structure function analysis of the catalytic subunit polymerase subdomain of the human mitochondrial DNA polymerase (pol  $\gamma$ ) showed that four Alpers syndrome mutations greatly reduced biochemical activity. The 99 percent activity loss in purified, recombinant forms of pol  $\gamma$  compared to the wild type polymerase (wt) would severely impair mitochondrial DNA replication.

The four disease point mutations are in highly conserved regions of the thumb subdomain of the polymerase domain of POLG, the gene encoding pol  $\gamma$ . Recombinants of two other Alpers mutations in less conserved regions of the adjacent palm subdomain retained 50-70 percent wild-type activity.

All replication and repair of mitochondrial DNA is done by pol  $\gamma$ . Mutations in *POLG* can impair the polymerase leading to mitochondrial diseases such as Alpers syndrome, an autosomal recessive disease with early onset mitochondrial DNA depletion. Mitochondria make over 90 percent of the energy needed by cells to function. Seriously impaired mitochondrial function can be fatal.

The NIEHS researchers showed that the mutants retained the wild type physical and functional relationships in the interaction with p55, a pol  $\gamma$  accessory subunit, had no misinsertion fidelity defects, and were properly folded with secondary structure similar to the wild-type enzyme. Differences in mutant protein DNA binding suggest a possible orientation of the polymerase to DNA during catalysis.

*Citation:* Kasiviswanathan R, Longley MJ, Chan SS, Copeland WC. 2009. Disease mutations in the human mitochondrial DNA polymerase thumb subdomain impart severe defects in mitochondrial DNA replication. J Biol Chem 284(29): 19501-19510.

Article in August Environmental Factor

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#### Mi-2/NuRD Is Part of a Novel Chromatin Assembly Pathway

The chromatin remodeling complex, Mi-2/NuRD, mobilizes nucleosomes through the Mi-2 ATPase subunit and deacetylates histones through the histone deacetylase (HDAC) subunit, but recent work has determined that the complex is also involved in the maturation and maintenance of heterochromatin in rapidly proliferating lymphoid cells. Investigators at NIEHS, Duke University and Emory University School of Medicine have shown that Mi-2/NuRD localizes to pericentromeric heterochromatin on human chromosomes 1, 9 and 16 during late S phase. The association occurs in some but not all cell types.

The research team used immunofluorescence and fluorescence *in situ* hybridization to visualize where Mi-2/NuRD localized within lymphoid cells. The NuRD bodies were present in a variety of B lymphocyte-derived cell lines as well as primary human cells. NuRD localized to heterochromatin that contained HP1 proteins and histone H3 trimethylated at lysine 9. In contrast, heterochromatin that lacked NuRD bodies differed in composition and instead assembled Polycomb proteins.

The research suggests the NuRD bodies are cytologic markers of a novel chromatin assembly pathway used by lymphoid cells at pericentromeric heterochromatin.

Citation: Helbling Chadwick L, Chadwick BP, Jaye DL, Wade PA. 2009. The Mi-2/NuRD complex associates with pericentromeric hetrochromatin during S phase in rapidly proliferating lymphoid cells. Chromosoma 118(4): 445-457.

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#### Web-Based SNP Tools Offer Unique Usability Features

NIEHS researchers have developed a set of single nucleotide polymorphism (SNP) selection tools that allow investigators to select SNPs using results from genome-wide associated studies (GWAS), linkage disequilibrium (LD) and predicted functional characteristics of both coding and non-coding SNPs. The tools are web based and may be used for small or large-scale SNP selection.

The authors designed the application, SNPinfo, to have three pipelines for SNP selection based on candidate genes, whole genome and linkage regions, with options to combine all three pipelines. In addition, the tools incorporate functional predictions of protein structure, gene regulation, splicing and miRNA binding and the ability to consider whether the alternative alleles of a SNP are likely to have differential effects on function.

As a validation step the authors show that a very small panel of SNPs chosen with the application captures most of the SNPs subsequently shown to be associated with disease. A variety of tools on the web site allows investigators to easily see all of the SNPs in a gene, their frequency in different populations, linkage disequilibrium, predicted functional consequences and sequence context. Public access to the site is at <a href="https://www.niehs.nih.gov/snpinfo">www.niehs.nih.gov/snpinfo</a>, and help files on the site provide a useful introduction to the different tools.

Citation: Xu Z, Taylor JA. 2009. SNPinfo: integrating GWAS and candidate gene information into functional SNP selection for genetic association studies. Nucl Acids Res 37: W600-W605; doi:10.1093/nar/gkp290 (Web Server Issue).

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)

### **Inside the Institute**

#### A Community of Support for the Summers of Discovery Students

By Laura Hall

For this year's Summers of Discover interns, the July 29 Poster Session was the culmination of four to six weeks of experimental research. The posters were also the result of special efforts made by many members of the NIEHS community to provide an enriching experience for the high school, undergraduate and graduate school students.

The program allows the young interns an opportunity to experience what being a scientist is really like and to fulfill one of the ongoing NIEHS missions – to mentor and train future scientists.

It is not just mentors in the labs who are involved. Linda Birnbaum, Ph.D., director of NIEHS and NTP, took time out of her busy schedule to talk to the students about their projects when they were setting up their posters. Deputy Scientific Director Bill Schrader, Ph.D., explained poster presentation skills.



Brittany Hopkins stood by her poster displaying her research using a mouse model of Ellis-van Crevald syndrome. She discovered that in research "you have to learn to fix problems... and sometimes you have to do things over and over again before you get it right." (Photo courtesy of Steve McCaw)

Twenty postdoctoral fellows judged the posters using 50 criteria. Acting laboratory branch chiefs gave special seminars on research at NIEHS. Staff scientists made presentations on research and career options. The students had special classes in laboratory skills. Debbie Wilson, coordinator of the 2009 Summers of Discovery Program, and Diane Klotz, Ph.D., director of the NIEHS Office of Fellows' Career Development, were involved in planning and scheduling all aspects of the program.

For the laboratory technicians, postdoctoral fellows and staff scientists involved, it takes work to mentor a student. Wes Gladwell, senior biologist in the Environmental Genetics Group who mentored Alexandra Levitt, explained, "You've got four to six weeks to train them and finish a project..., so you've got to figure out what they can actually do in that period to get it done."



The 2009 Summers of Discovery students posed with their mentors and supporters for the traditional group photo. (Photo courtesy of Steve McCaw)

Others in the laboratory help out with the training, particularly when the mentor is unavailable. The students "learn something from everyone." said Sylvia Hewitt, biologist in the Receptor Biology Group.

For those who enjoy teaching, the rewards can be great. Ron Cannon, staff scientist in the Intracellular Regulation Group, mentored North Carolina State University (NCSU) undergraduate John Peart, who won one of the Best Poster awards (see related story). Cannon enjoyed seeing the students "flourish and develop...[I]n some cases they come up with ideas that you would not have thought of because they're thinking outside of the box. That to me is very, very satisfying."

Valuable research can be generated. Gladwell said, "We had 34 in-bred [mouse] strain screens that we had done over the three years so we had all the phenotype data to look at...but she [Levitt] helped me compile all of it and was probably learning the software as fast as I was."

Susan Elmore, NTP pathologist and staff scientist, mentored Laura Crawford, Ph.D., an NCSU veterinary student Elmore considered to be "exceptional." In two summers in the program, Crawford completed a high-resolution color histology atlas of normal liver and biliary systems in developing mice. "It will be one of the prized resources in the toxicologic-pathology community that everybody uses" for phenotyping transgenic mouse embryos, declared Elmore.

It is a great opportunity for the students, particularly for those trying to decide on their career track. Gladwell said, "I really think kids get to decide if science is for them or not for them. I think a lot of kids never really even considered research [before]." For more independent students, first authorship on a scientific paper is a possibility. Crawford is first author on the histology atlas paper resulting from her work, which is now ready for internal review.

Speaking of his own experience this summer, Cannon said, "I had a mentor...[who] said, 'You build a boat and you push it off and watch it sail.' So I think that's what we're doing here in the mentoring program." It takes a community of "boat builders" to nurture future scientists. For the many involved, from the director to the laboratory technician, it's well worth the effort.

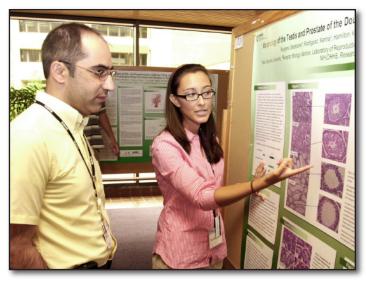
(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)



Director Linda Birnbaum enjoyed a discussion with a research student. "I really think that reaching out to the next generation of biomedical researchers is one of our responsibilities as senior investigators," she said. "We never know when we might influence someone to begin a brilliant scientific career." (Photo courtesy of Steve McCaw)



Veteran intern Alexandra Levitt, center, worked with Principal Investigator Steve Kleeberger, Ph.D., right, on a continuing project. Together with her mentor, Wes Gladwell, left, they began analyzing the data this summer. (Photo courtesy of Steve McCaw)



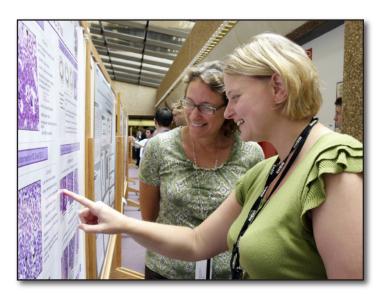
Clinical researcher Stavros Garantziotis, M.D., watched as Stephanie Rodgers explained her morphology work on double estrogen receptor knockout mice. Rodgers was mentored by Sylvia Hewitt, a biologist in the Receptor Biology Group. (Photo courtesy of Steve McCaw)



Ashwin Peres-da-Silva explains that his study on SIRT1 has "been really fun though it's really challenging. It really gets you to think about stuff, so I've enjoyed it a lot." (Photo courtesy of Steve McCaw)



Sung-Yong Hwang, Ph.D., foreground, has an intent discussion with Natisha Mandadi on her research on nucleotide excision repair of thymine dimers. Mandadi said this summer "made me feel more like I want to do research... It's fun to figure out the puzzle... to figure out the best way to work an experiment." (Photo courtesy of Steve McCaw)



Laura Crawford, right, posed by her poster with her mentor, Susan Elmore. "To have a summer student come in and get this much done in two summers was really unbelievable. [The] contribution to the tox[icolic]-path[ology] community is huge," said Elmore. (Photo courtesy of Steve McCaw)



Visiting Fellow Deepti Dwivedi, Ph.D., left, listened as Alan Chin explained that cadmium exposure may hasten the formation of cancerous stem cells from normal stem cells. Chin said, "I definitely like research a lot more now because of the experience I had here." (Photo courtesy of Steve McCaw)



Matthew Hunt, left, told Yuan Liu, Ph.D., about his research on the arc protein. Hunt said, "There's a lot more to it [being a scientist] than I thought [and] not everything is going to go as planned, so [with] each experiment you'll think of something new that next time you'll need to plan for." (Photo courtesy of Steve McCaw)

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#### **Employees Recognized for Decades of Service**

By Eddy Ball

In another first for NIEHS and the National Toxicology Program, Director Linda Birnbaum, Ph.D., honored employees for their decades of service with their own dedicated ceremony and reception in Rodbell Auditorium August 7. In past years, employees honored for years of service were recognized at the end of the annual Director's Awards ceremony each December.

In lighthearted opening remarks, Birnbaum praised the employees for their "achievement as survivors" and added on a more serious note that in another month she'll qualify herself for a 30-year service award. "Hopefully, by this time next year," she continued," I'll be receiving my own service award."

"I'm going to make this an annual event," she explained. "Years of service is certainly an important achievement, and it should be singled out for recognition." Birnbaum also said that retirees will be recognized at the Director's Awards ceremony.



As she did with Alyce Bradbury, left, Birnbaum presented an award to each winner as Kleeberger, on stage, prepared to call the next name. (Photo courtesy of Steve McCaw)

Ably assisted by Acting Deputy Director Steve Kleeberger, Ph.D., Birnbaum handed a special service plaque to each awardee and posed for individual photos. Afterwards, the groups of awardees, recognized for 10, 20 or 30 years of service, posed with their similarly honored colleagues for group pictures.

Following the ceremony awardees and co-workers enjoyed cake, ice cream and fellowship in the lobby where they talked and mingled.



Holding up their awards for 20 years of service in the front row are, left to right, Wendy Jefferson, Freya Kamel, Melissa Gentry, Rhonda Carroll, Kim Peterson and Katarzyna Bebenek. In the back row, left to right, are Veronica Godfrey, Michelle Owens, Kathy Crabtree, Mitsue Parrish and Stephen Cannon. Not shown: Michael Loewe, Norris Flagler, Sam Wilson, Donna Roach and James Bryant. (Photo courtesy of Steve McCaw)



Sherry Coulter, left, and 30-year veteran Clyde Hasty enjoyed conversation and refreshments after the ceremony. (Photo courtesy of Steve McCaw)



Ten-year veterans posed for a group photo. Shown, left to right, in the front are Edith Lee, Kim McAlister, Alyce Bradbury, Tanya Shields, Mitzie Walker and Andrea Moon. In the back row, left to right, are Lutz Birnbaumer, Aaron Nicholas, Erin Dooley, Kim Gray, Heather Jensen, Craig Wladyka, Paula Juras and Greg Scott. Not shown: Dorcus Joya, Gloria Nicholson, Kimberly Jones, Patrick Barbour, Tanya Tillett (Photo courtesy of Steve McCaw)



Thirty-year employees posed with their well deserved plaques. In the front row, left to right, are J. Michael Sanders, Vicki Grigston, Clyde Hasty, Bob Langenbach, Nancy Mitchell and Susan Sherron. Shown in the back row, left to right, are Clifton Baldwin, Anton Jetten, Chris Portier, Vondia Malone and Lisa Rogers. Not shown: Allen Wilcox, Jimmy Washington, Mary Gant, Masahiko Negishi, Nell Boyd. (Photo courtesy of Steve McCaw)



Friends and colleagues joined the award recipients — both to celebrate their accomplishment and indulge in the refreshments. (Photo courtesy of Steve McCaw)

#### **Work/Life Event Focuses on Community Resources**

By Eddy Ball

NIEHS held its most recent Work/Life event on August 6 with a mid-day Community Resources Festival in Rodbell Auditorium. Representatives of NIEHS and local organizations staffed some 22 tables, handing out snacks, freebees and information as employees and contractors browsed, talked and asked questions.

While several of the displayers were veterans of earlier Work/Life events, the NIEHS Employee Services staff brought in some new people to introduce employees and contractors to lesser known homegrown support programs and educational opportunities in the Triangle. These included A Place for Mom, a clearinghouse for information about assisted care options; Cornucopia House, a cancer support center in Chapel Hill; and the North Carolina Library for the Blind and Physically Handicapped, a special public library for people who cannot use regular printed materials.

Also new to the Work/Life circuit was the NIEHS Assembly of Laboratory Staff (AoLS), an organization started earlier this year to represent the interests of lab technical employees. AoLS joined other NIEHS organizations at the festival, including the Quality Council, the Office of Communications and Public Liaison, Health and Safety Branch, Diversity Council, Disability Advocacy Committee and American Federation of Government Employees Local 2923.

Doing their part to support the theme of balancing work and life were representatives of educational and entertainment groups that were new to NIEHS, such as the North Carolina Museum of History and Sarah B. Duke Gardens. A few other familiar



Gathered at the AoLS table are, left to right, Page Myers, Durham Bulls mascot Wool E. Bull, Gina Goulding, Dick Sloane in back, Paula Brown and Laura Miller DeGraff. (Photo courtesy of Steve McCaw)



As the Festival wound down, left to right, organizer Dona McNeill took a breather with Gerard and Juanita Roman. (Photo courtesy of Steve McCaw)

organizations were also on hand, with staff from with Durham Parks and Recreation and the Durham Bulls.

Even if some resources haven't changed much recently, people's lives can. Staff at tables for First Environments, the NIEHS/EPA childcare facility on campus, and tables on boating and cycling safety kept busy explaining their programs as the crowds passed through the auditorium.

According to Employee Services Manager Dona McNeill, the program is always glad to receive new ideas for Work/Life events. McNeill and co-organizer Intern Jenn Evans invite suggestions about new themes and resource groups for future events.



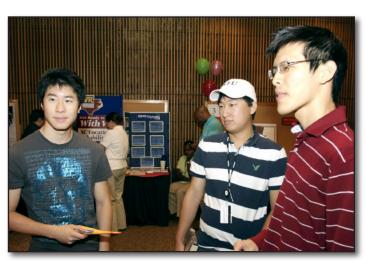
Research Biologist Donna Stefanick, standing foreground, thumbed through maps and brochures from such local attractions as North Carolina State University's J.C. Raulston Arboretum in Raleigh. (Photo courtesy of Steve McCaw)



For Intern Jenn Evans, above, the Festival was the culmination of her summer's work at NIEHS. Evans is a senior at the University of North Carolina at Greensboro majoring in Human Development and Family Studies. (Photo courtesy of Steve McCaw)



NIEHS Office of Communication and Public Liaison (OCPL) employees Laura Hall, left, and Myra Westmoreland talked at the OCPL display. (Photo courtesy of Steve McCaw)



Left to right, Summers of Discovery interns Alan Chin, Patrick Li and Wayneho Kam dropped by to check out the Festival scene. (Photo courtesy of Steve McCaw)

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